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Human exposure to mercury and its hematological effects: a systematic review

Exposição humana ao mercúrio e seus efeitos hematológicos: uma revisão sistemática

Exposición humana al mercurio y sus efectos hematológicos: una revisión sistemática

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Abstract

Mercury is a metal found in the environment from natural and anthropogenic sources. It is highly toxic to ecosystems and living beings. Most human exposures come from ingestion of contaminated seafood, outgassing from dental amalgam or occupational exposure (e.g. gold mining), among other cases. Large populations are exposed to mercury, making it a very important issue from the public health perspective. Adverse health effects are commonly seen in the nervous system, but every organ is a potential target, such as the bone marrow. The main goal of this study was to assess the available evidence on human exposure to mercury and its hematological effects. A search strategy was constructed, including key terms (MeSH, text word and equivalents) for querying 2 repositories of master dissertation and PhD thesis (Fiocruz/ARCA and University of São Paulo) and 4 different electronic databases: BVS/LILACS, MEDLINE/PubMed, Scopus and TOXLINE/NIH, for articles published from 1950 to February 2018. There was no language restriction and a tool (EPHPP) was used to assess the quality of included studies. According to pre-established criteria, 80 studies were retrieved, all of them observational (48 case reports, 24 cross-sectional, 6 case series and 2 cohorts), comprising 9,284 people. Despite the fact that most exposed ones (6,012) had normal blood cell count and mercury hematological effects did not seem very usual (1,914 cases: 14 severe and 29 deaths), three studies reported association (β) for anemia, lymphopenia, neutrophilia and basophilia. We concluded that the gathered information pointed to mercury hematotoxic effects, some of them may be serious and even fatal.

Mercury Poisoning; Heavy Metal Poisoning; Mercury; Blood Cell Count

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Introduction

Mercury is a heavy metal considered as the most toxic non-radioactive element in the world. It is ubiquitous, indestructible and exists in three forms in nature: inorganic, metallic and organic [1]. It is released to the atmosphere from four different sources: (i) primary natural (e.g. volcanic and geothermal activities), responsible for 10%; (ii) primary anthropogenic (e.g. mining and fossil fuel extraction, including oil, gas and coal); (iii) secondary anthropogenic (mercury-dependent artisanal and small scale gold mining sector [ASGM], several industrial processes including chlor-alkali industry), both anthropogenic responsible for 30%; and (iv) remobilization and re-emissions (wildfires, forest clearing, biomass burning), responsible for 60% [2]. Because it is a widespread environmental toxicant, humans are unable to avoid exposure to its forms [3] and the main sources are: fish and shellfish consumption, outgassing from dental amalgam, vaccines containing thiomersal and occupational exposure (agricultural products, industry and gold mining) [4]. Specifically in relation to the latter, ASGM is considered the number one anthropogenic mercury pollutant in the world, responsible for 37% (410 to 1,400 tones/year) of its emissions to air and water worldwide. It poses a risk not only to miners, estimated at 10 to 19 million workers, of which 5 million are women and children, in more than 70 countries, but also to the environment and general population by water and air [2,5]. Such large variation of human exposure to mercury makes it a very important issue from the public health perspective [6,7].

All forms of mercury could poison cellular function by altering the tertiary and quaternary structure of proteins and membrane permeability due to its affinity for sulfhydryl and selenohydryl groups. As a consequence it can potentially impair function of any organ [8,9]. Its adverse effects on human health may induce over 250 symptoms. The main ones are from nervous, renal, cardiovascular, respiratory systems, and skin, but any organ may be a target, such as the bone marrow [9]. The hematological system, due to its intense cellular proliferation, is quite sensitive to the action of a variety of substances, such as benzene [10]. However, there is sparse information and research about mercury's hematotoxicity on humans, despite its wide exposure [11]. Most of them come from occupational settings [12,13], in vitro [14,15] and animals studies [16,17].

The aim of this systematic review was to assess the available evidence on human exposure to mercury and its hematological effects.

Methods

This systematic review followed the precepts established by the PRISMA model [18] and had a PROSPERO register: CRD42018086389.

Data sources, search strategy and study selection

The selection criteria were based on PICOS' acronymous [19]: "Does human exposure to mercury lead to hematological effects?" and included all studies (except textbook, author's opinion and review) regarding human exposure to mercury and hematological effects, published between 1950 and February 2018. Hematological effects were considered as any blood cell alteration concerning number [20] and the normal values of mercury on biological matrices were those presented by the authors.

We developed a search strategy including key terms (MeSH, text word and equivalents) for querying four different electronic databases (BVS/LILACS; MEDLINE/PubMed; Scopus; and TOXLINE/NIH) and two Master dissertation/PhD thesis databases (Fiocruz/ARCA and University of São Paulo). There were four search strategies containing the descriptors according to database and repositories. For BVS/LILACS: "mercúrio" AND "anemia" OR "leucopenia" OR "basopenia" OR "eosinopenia" OR "neutropenia" OR "linfopenia" OR "monocitopenia" OR "trombocitopenia" OR "policitemia" OR "leucocitose" OR "basofilia" OR "eosinofilia" OR "neutrofilia" OR "linfocitose" OR "monocitose" OR "trombocitose" OR "hemograma completo". For MEDLINE/PubMed: "anemia" OR "leukopenia" OR "thrombocytopenia" OR "eosinopenia" OR "basopenia" OR "monocytopenia" OR "polycythemia" OR "leukocytosis" OR "thrombocytosis" OR "eosinophilia" OR "basophilia" OR "neutrophilia" OR

"monocytosis" OR "blood cell count" AND "mercury". For TOXLINE/NIH, the search was made in a binary way: anemia and mercury/leukopenia and mercury. For the two repositories: "mercúrio" and "efeitos hematológicos". Reference lists were also searched for relevant studies. No restrictions were applied concerning language and translation was done whenever necessary. Both authors (A.S.V. and E.P.M.) followed the same schedule independently: first they reviewed the title, then the available abstract, soon after the analysis of full text, and finally the search for reference. Any discrepancy in the search results not solved between A.S.V. and E.P.M. was planned to be discussed with a third author (C.I.R.F.A.). In order of priority, we excluded: non-human studies; without mercury exposure; lacking hematological effect; textbook, author's opinion and review papers (type of study); and those published before 1950. To determine agreement between the two raters, Cohen's kappa statistic was used for each step.

Data extraction

The extraction process was also done independently and included: author, year, place, journal, data base, type of study, substance, exposure (local and duration), population (number, exposed versus non exposed, age, sex), hematological outcome (primary or secondary), death, blood cell count, bone marrow biopsy, mercury (sample, level, method) and statistical analysis. Once more, Cohen's kappa statistic was used to evaluate an inter-rater agreement.

Study quality assessment

To assess the quality/bias risk of the selected studies, we chose a tool known as Effective Public Health Practice Project (EPHPP) [21]. This quality assessment tool for quantitative studies has eight components ratings: (a) selection bias; (b) study design; (c) confounders; (d) blinding; (e) data collection methods; (f) withdrawals and drop-outs; (g) intervention integrity; and (h) analyses. Items from "a" to "f" are rated as strong (1), moderate (2) or weak (3). There is a dictionary to correctly rate each section. These six items are included in global rating, ranked as follows: strong must not have no weak ratings; moderate may have one weak rating, and weak may have two or more weak ratings. At the end there is an item for discrepancy between both reviewers that indicate the reason for discrepancy: oversight, differences in interpretation of criteria and differences in interpretation of study. That will lead to a final decision of both reviewers.

The results were summarized in a descriptive manner for occupational and non-occupational exposure data, due to toxicological differences between them.

Results

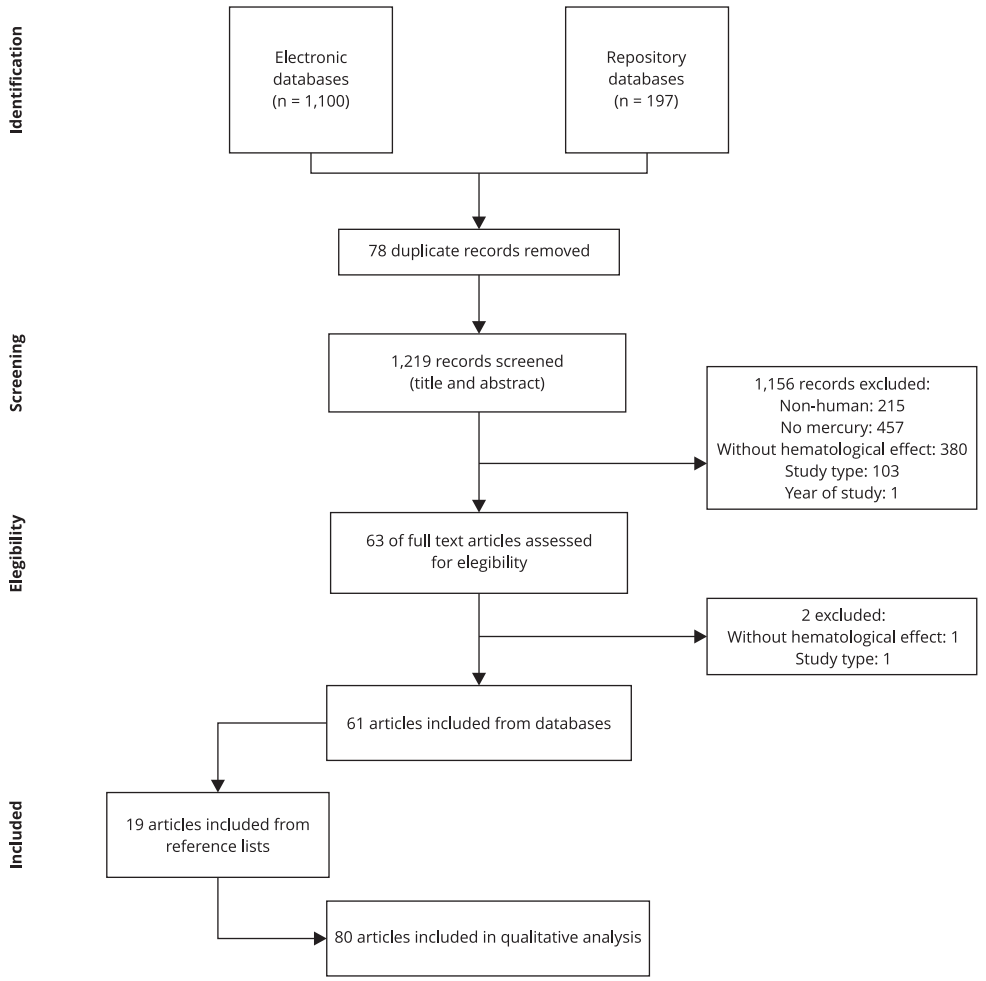
The search yielded 1,297 citations as of February 14th 2018, 323 from BVS/LILACS, 142 from MEDLINE/PubMed, 525 from Scopus, 110 from TOXLINE/NIH, 197 from Fiocruz/ARCA and none from the University of São Paulo. After 78 duplicates were removed, 1,219 records were screened based on review of titles and abstracts. Thereafter 63 full texts of articles were assessed for eligibility. The search to identify any missed report or citations resulted in selection of 80 articles: 61 from electronic databases search and 19 from reference lists. The reasons for 1,158 articles exclusion were: no mercury (457), without hematological effect (381), non-human (215), study type (104) and year of study (1) (Figure 1).

The Cohen's kappa statistic was considered as almost perfect (0.98, 95%CI: 0.91; 1.0, $p < 0.001$) during screening title and abstract and substantial (0.76, 95%CI: 0.54; 0.98, $p < 0.001$) during extraction process. There was no more disagreement at other steps.

All were observational studies comprising 48 case reports (42 comprising one person/52.5%), 24 cross-sectional (12 containing control group), six case series and two cohorts. The study design was reported according to authors' description. They were published between 1950 and 2018, with an increasing pattern in the last three decades (1950: 4 studies; 1960: 5; 1970: 7; 1980: 10; 1990: 15; 2000: 19; and 2010: 20). They were done in 34 different countries (14 in the USA) on the five continents and

Figure 1

Flowchart showing the selection of studies for the systematic review.



the main language was English (63). However, hematological effect was the primary outcome only in 14 studies (17.5%).

A total of 9,284 people were evaluated: 6,601 from non-occupational (60 studies) and 2,605 from occupational (23 studies) exposure. There was no report on 78 times. Three articles had both types, so there was a split between persons, according to it.

There were differences of age and sex distribution between exposure: at non-occupational, children and teenagers were the majority (4,982/75.47%) while at occupational, adults were (1,752/67.26%). According to sex: women were predominant (3,640/55.14%) at non-occupational and men were at occupational settings (1,402/53.84%).

The non-occupational pathways of exposure were: food (5,243), home near gold mining plus food (291), amalgam (454), environmental (82), medicine (54), bringing mercury home (29), suicide attempt (15), school (2), maternal exposure (2), aesthetical (1) and thermometer (1). The occupational pathways were: agriculture (1,274), gold mining (230), chlorine alkali industry (215), lamp factory (209), mix of three places: chlorine alkali industry, lamp factory and dentist's office (71), dentist's office (47) thermometer factory (2), research lab (1), fur-cleaning establishment (1) and compressor use (1). The main

pathways of exposure among children and teenagers were: food (4,800), environmental (82), home near gold mining plus food (70) and bringing mercury home (14).

Three distinctive groups that are more susceptible to chemical substances, due to physiological characteristics and proportional high exposure levels, received attention on 33 studies: 23 for exposed occupational populations (13 cross-sectional of which seven with exposure and control groups), eight for children and teenagers (six cross-sectional and two cohorts), one for pregnant, neonates and children (cross-sectional) and one for pregnant (cross-sectional).

Chronic exposure was the main type for both, comprising 33 non-occupational (6,127 persons) and 16 occupational (2,041 persons) studies.

Hematological effects were described 2,376 times, in 69 studies comprising 1,914 cases (20.62%): 479 children and teenagers, 476 adults, 13 elderly and 946 not classified. Non-occupational exposure was the most frequent (1,111). Blood cell count was done in all cases and bone marrow biopsy in 13 times. Anemia (875), lymphocytosis (361) and lymphopenia (306) were the top three, although only anemia was the most common in both type of exposures. In fact, there was alteration of all bone marrow cellular series in mercury's presence (Table 1). In 1,567 of all cases (81.87%), mercury's exposure biomarker was above the recommended threshold. The blood cell count was normal in 7,250 times, where 6,012 individuals were exposed to mercury (75.85%).

Six out of seven studies reported lymphocytosis related to metallic or inorganic mercury exposure [13,22,23,24,25,26].

Fifteen studies, of which 14 are case reports [27,28,29,30,31,32,33,34,35,36,37,38,39,40] and one is cross-sectional [41], comprising 27 cases, reported some severe hematological effects associated to clinical condition, such as: cerebral or gastrointestinal bleeding related to thrombocytopenia (14) or aplastic anemia (2); multiple organ dysfunction syndrome and leukopenia (2) or hemolytic anemia (2) or aplastic anemia (1); renal insufficiency and thrombocytopenia (2) or leukemoid reaction (1); sepsis and aplastic anemia (2) or neutropenia (1). Mercury biomarker was measured 22 times [29,30,31,32,36,37,38,39,40,41] out of 27 and was always high according to values reported by the authors.

Death was reported 29 times, most of them at non-occupational settings (26), due to medicine use (19/26). In 19 times, the cause of death was directly related to hematological effect: 16 due to severe bleeding (thrombocytopenia [14] and aplastic anemia [2]) and three due to sepsis (neutropenia [1] and aplastic anemia[2]).

The authors of 38 studies hypothesized that mercury could be responsible for the hematological effect by direct toxicity to bone marrow (13), immunologic/hypersensitivity (9), apoptosis (5), chronic disease (3), immunologic/autoimmunity (3), inflammatory reaction (3), hemolysis (3), loss of blood (3), increased calcium content in cytoplasm (2), idiosyncrasy (2) and increased level of erythropoietin (1).

Statistical analysis concerning mercury exposure and hematological effect was reported in 17 studies as follows: 11 were mean difference (Student's *t*-test; Wilcoxon) [12,22,23,24,42,43,44,45,46,47,48]; eight (two data not shown) were correlation coefficient *r* (Pearson; Spearman) [12,22,23,24,43,44,49,50]; three were regression coefficient β (linear models) [51,52,53]; two (one data not shown) were prevalence [49,54] and one was odds ratio (data not shown) [48]. The results reported for mean difference were: four studies evaluated anemia and two did not find difference ($p = 0.05$ and $p = 0.183$) [42,48] and other two found it ($p = 0.016$ and $p < 0.05$) [43,47]; one study found difference for leukopenia and neutropenia ($p < 0.05$) [46]; five studies analyzed lymphocytes and three did not find difference (p not informed) [22,23,24] and one did find ($p < 0.05$) [12]; one study evaluated polycythemia and did find difference ($p < 0.05$) [45]. For correlation coefficient, two studies evaluated anemia and found moderate negative correlation ($r = -0.4208$, $p = 0.003$) [44] and no correlation ($r = 0.04$, p not informed) [49]; six studies analyzed lymphocytes and three found no correlation ($r = -0.077$, p not informed; *r* not informed; $r = -0.11$, 0.10, p not informed) [12,23,44] and other three found a weak to moderate positive correlation ($r = 0.3405$, $p < 0.05$; $r = 0.184$, $p < 0.05$; $r = 0.121$, $p = 0.049$) [22,24,50]. For regression coefficient, two studies found inverse association for lymphopenia ($\beta = -1.26$ [95%CI: -2.61; 0.08]; $\beta = 23\%$ [95%CI: -43; -4]) [51,52] and one for anemia ($\beta = -0.14$, $p = 0.04$) [53]. One found positive association for neutrophilia and basophilia ($\beta = 1.38$, 95%CI: 0.11; 2.65 and $\beta = 0.04$, 95%CI: -0.03; 0.11) [51]. For prevalence, one study reported 22% (95%CI: 18.0; 25.9) for anemia [54].

The characteristics of these studies are summarized in Tables 2 and 3.

Table 1

Hematological effects found in the studies according to exposure.

Hematological effect	Exposure	Cases
Anemia	Non-occupational	547
	Occupational	328
Polycythemia	Non-occupational	0
	Occupational	48
Leukopenia	Non-occupational	84
	Occupational	22
Leukocytosis	Non-occupational	23
	Occupational	3
Basopenia	Non-occupational	80
	Occupational	0
Basophilia	Non-occupational	191
	Occupational	0
Eosinophilia	Non-occupational	30
	Occupational	7
Neutropenia	Non-occupational	26
	Occupational	0
Neutrophilia	Non-occupational	199
	Occupational	5
Lymphopenia	Non-occupational	273
	Occupational	33
Lymphocytosis	Non-occupational	102
	Occupational	259
Monocytopenia	Non-occupational	56
	Occupational	0
Monocytosis	Non-occupational	24
	Occupational	0
Thrombocytopenia	Non-occupational	19
	Occupational	2
Thrombocytosis	Non-occupational	2
	Occupational	0
Pancytopenia	Non-occupational	5
	Occupational	1
Other (alteration of hematocrit and leukocytes)	Non-occupational	0
	Occupational	7
Total		**2,376**

The quality assessment for these studies was considered weak (3) according to EPHPP for 75 of them. Almost all component ratings were considered as weak (selection bias, study design, confounders and blinding) or not applicable (withdrawals and dropouts). There was no discrepancy between the two reviewers concerning component ratings.

Discussion

We identified 80 out of 1,219 studies of mercury exposure and hematological outcomes, including environmental studies of children, teenagers, adults and elderly, as well as occupational ones. However, there were only 14 studies that aimed at hematological effect as the primary outcome. All were observational comprising a total of 9,284 studied people, although 42 were case reports of just one person.

Table 2

Mercury's non-occupational exposure studies.

Study (year)	Country	Study characteristics [design/number/exposure]	Population [age/sex]	Mercury level	Hemtologic effect	Statistical analysis	EPHPP tool
Bender et al. [27] (1950)	USA	Case report; n = 1; non-occupational (medicine)/ chronic	Female (61y)	NI	Anemia = 1, leukopenia = 1, neutropenia = 1	NA	3
Butt & Simonsen [41] (1950)	USA	Cross-sectional; n = 134, no control (occupational = 1, non-occupational = 55, NI = 78); non-occupational (medicine + environment + maternal exposure)	Female = 22, male = 42, NI = 69 (< 1-81y)	High	Thrombocytopenia = 12	ND	3
Doolan et al. [73] (1953)	USA	Case report; n = 1; non-occupational (suicide)/chronic	Female (28y)	NI	Anemia = 1	NA	3
Portwich & Maron [28] (1959)	Germany	Case report; n = 1; non-occupational (medicine)/ chronic	Female (64y)	NI	Thrombocytopenia = 1	NA	3
Larsen et al. [82] (1963)	USA	Case report; n = 2; non-occupational (medicine)/acute	Female = 1, male = 1 (55y, 69y)	NI	Leukocytosis = 1, normal = 1	NA	3
Ross [83] (1964)	USA	Case report; n = 1; non-occupational (medicine)/ chronic	Male (4y)	High	Leukocytosis = 1	NA	3
Wilson [29] (1966)	UK	Case report; n = 1; non-occupational (medicine)/ chronic	Male (77y)	High	Anemia = 1, leukopenia = 1, thrombocytopenia = 1	NA	3
Johnson et al. [30] (1978)	USA	Case report; n = 1; non-occupational (medicine)/ chronic	Female (3y)	High	Anemia = 1, leukopenia = 1, neutropenia = 1	NA	3
Hannigan [84] (1978)	UK	Case report; n = 1; non-occupational (suicide)/chronic	Male (34y)	High	Normal = 1	NA	3
Murphy et al. [31] (1979)	UK	Case report; n = 1; non-occupational (medicine)/acute	Male (35y)	High	Anemia = 1, leukocytosis = 1, neutrophilia = 1, thrombocytopenia = 1	NA	3
Slee et al. [32] (1979)	Netherlands	Case report; n = 1; non-occupational (medicine)/acute	Female (59y)	High	Anemia = 1, leukopenia = 1, thrombocytopenia = 1	NA	3
Wright et al. [85] (1980)	UK	Case report; n = 1; non-occupational (suicide)/acute	Male (17y)	NI	Normal = 1	NA	3
Lien et al. 86 (1983)	Canada	Case series; n = 7 (occupational = 1, non-occupational = 6); non-occupational (home)/acute	Female = 1, male = 2, NI = 3 (< 2-28y)	High = 6	Leukocytosis = 6	NA	3
McNeil et al. [87] (1984)	UK	Case series; n = 4; non-occupational (home)/chronic	Female = 2, male = 2 (10-41y)	High	Normal = 4	NA	3
Foulds et al. [88] (1987)	USA	Case report; n = 1; non-occupational (home)/chronic	Female (< 3y)	High	Normal = 1	NA	3

(continues)

Table 2 (continued)

Study (year)	Country	Study characteristics [design/number/exposure]	Population [age/sex]	Mercury level	Hemtologic effect	Statistical analysis	EPHPP tool
Lauwerys et al. [25] (1987)	Belgium	Case report; n = 1; non-occupational (aesthetic/ maternal exposure)/chronic	Male (< 1y)	High	Anemia = 1, leukocytosis = 1, lymphocytosis = 1	NA	3
Oliveira et al. [89] (1987)	UK	Case report; n = 1; non-occupational (aesthetic)/ chronic	Female (46y)	High	Anemia = 1	NA	3
Tunnessen et al. [78] (1987)	USA	Case report; n = 1; non-occupational (school)/chronic	Male (< 2y)	High	Leukocytosis = 1, Eosinophilia = 1, thrombocytosis = 1	NA	3
Murray & Hedgepeth [90] (1988)	USA	Case report; n = 1; non-occupational (suicide)/chronic	Male (25y)	High	Anemia = 1, neutrophilia = 1	NA	3
Oluwole et al. [42] (1989)	Nigeria	Cross-sectional; n = 21 (no control); non-occupational (environment)/chronic	Male = 21 (3-12y)	High = 1, normal = 20	Anemia = 10, normal = 11	t-test, no mean difference, $p < 0.05$	3
Siblerud [43] (1990)	USA	Cross-sectional; n = 101 (exposed = 50, not exposed = 51); non-occupational (amalgam)/chronic	Female = 60, male = 41 (exposed x = 22y, not exposed x = 23y)	NI	Anemia = 15, normal = 86	Mean difference, $p = 0.016$; Pearson $r = -0.4208$, $p = 0.003$	3
Montoya-Cabrera et al. [26] (1991)	Mexico	Case report; n = 1; non-occupational (medicine)/acute	Female = 1 (< 1y)	High	Anemia = 1, lymphocytosis = 1	NA	3
Schwartz et al. [81] (1992)	USA	Case series; n = 4; non-occupational (home)/acute	Female = 1, male = 3 (< 4y-adults)	High	Anemia = 1, leukopenia = 1, thrombocytopenia = 1, normal = 3	NA	3
Pavithran [33] (1994)	India	Case report; n = 1; non-occupational (medicine)/ chronic	Female (29y)	ND	Anemia = 1, leukopenia = 1, thrombocytopenia = 1	NA	3
Alvarado et al. [34] (1995)	Costa Rica	Case report; n = 2 (occupational = 1, non-occupational = 1); non-occupational (medicine)/ chronic	Male (25y)	NI	Leukocytosis = 1, neutrophilia = 1	NA	3
Fuortes et al. [39] (1995)	USA	Case report; n = 3; non-occupational (home)/chronic	Female = 1, male = 2 (10y, 12y, 17y)	High	Anemia = 1, leukocytosis = 1, eosinophilia = 2, thrombocytopenia = 2, normal = 1	NA	3
Dell'Omo et al. [91] (1997)	Italy	Case report; n = 1; non-occupational (suicide)/chronic	Male (34y)	High	Normal = 1	NA	3
Dada et al. [35] (1999)	South Africa	Case report; n = 1; non-occupational (medicine)/acute	Male (21y)	NI	Anemia = 1, leukopenia = 1, thrombocytopenia = 1	NA	3
Chodorowski & Anand [92] (2000)	Poland	Case report; n = 2; non-occupational (suicide)/acute	Male = 2 (19-59y)	High	Normal = 2	NA	3

(continues)

Table 2 (continued)

Study (year)	Country	Study characteristics [design/number/exposure]	Population [age/sex]	Mercury level	Hemtologic effect	Statistical analysis	EPHPP tool
Tschanz & Prins [77] (2000)	Switzerland	Case report; n = 1; non-occupational (medicine)/acute	Female (29y)	NI	Leukocytosis = 1, eosinophilia = 1	NA	3
González et al. [93] (2001)	Venezuela	Case report; n = 1; non-occupational (medicine)/acute	Female (3y)	Normal	Anemia = 1, leukocytosis = 1, neutrophilia = 1, thrombocytosis = 1	NA	3
Deschamps et al. [94] (2002)	France	Case report; n = 1; non-occupational (suicide)/chronic	Male (41y)	High	Normal = 1	NA	3
Langworth et al. [95] (2002)	Sweden	Cross-sectional; n = 379 (no control); non-occupational (amalgam)/chronic	Female = 263, male = 116 (x = 46y)	High	Anemia = 6, normal = 373	ND	3
Winkler et al. [96] (2002)	Austria	Case report; n = 1; non-occupational (suicide)/acute	Male (22y)	High	Anemia = 1	NA	3
Kouyn et al. [97] (2004)	Turkey	Case report; n = 3; non-occupational (home)/chronic	Female = 1, male = 2 (11y, 13y, 16y)	Normal = 1, high = 2	Normal = 3	NA	3
Glezos et al. [98] (2006)	Canada	Case report; n = 1; non-occupational (home)/acute	Male (43y)	High	Anemia = 1	NA	3
Maramba et al. [76] (2006)	Philippines	Cross-sectional; n = 140 (exposed = 100, not exposde = 40); non-occupational (gold minig = food)/chronic	Female = 70, NI = 70 (35 < 1y, 35 < 2y, 70 x = 28y)	Normal, high *	Anemia = 140, eosinophilia = ?	ND	3
Frisk et al. [46] (2007)	Sweden	Cross-sectional; n = 46 (exposed = 24, not exposed = 22); non-occupational (amalgam)/acute	Adults = 46	Normal	Leukopenia = 24, neutropenia = 24, basopenia = 24, lymphopenia = 24, eosinophilia = 24, monocytosis = 24, normal = 22	Wilcoxon's sign rank, mean difference, $p < 0.05$	3
Matushita et al. [99] (2007)	Brazil	Case report; n = 1; non-occupational (suicide)/chronic	Male (29y)	High	Normal = 1	NA	3
Bamonti et al. 100 (2008)	Italy	Case report; n = 1; non-occupational (amalgam)/acute	Female (63y)	Normal	Anemia = 1, leukocytosis = 1, neutrophilia = 1, lymphopenia = 1	NA	3
Girault et al. [101] (2008)	France	Case report; n = 1; non-occupational (medicine)/acute	Female (66y)	High	Neutrophilia = 1, lymphopenia = 1	NA	3
Berrouet Mejía et al. [102] (2008)	Colombia	Case report; n = 1; non-occupational (suicide)/chronic	Female (16y)	High	Anemia = 1, leukocytosis = 1, neutrophilia = 1	NA	3
De Palma et al. [36] (2008)	Italy	Case report; n = 1; non-occupational (suicide)/acute	Female (30y)	High	Anemia = 1, leukocytosis = 1	NA	3
Erkek et al. [40] (2010)	Turkey	Case report; n = 1; non-occupational (environment)/ acute	Female (10y)	High	Anemia = 1	NA	3
Sarikaya et al. [103] (2010)	Turkey	Case report; n = 1; non-occupational (school)/acute	Female (36y)	NI	Normal = 1	NA	3

(continues)

Table 2 (continued)

Study (year)	Country	Study characteristics [design/number/exposure]	Population [age/sex]	Mercury level	Hemtologic effect	Statistical analysis	EPHPP tool
Al-Sinani et al. [79] (2011)	Oman	Case report; n = 1; non-occupational (medicine)/ chronic	Female (12y)	High	Leukocytosis = 1, eosinophilia = 1	NA	3
Plante et al. [49] (2011)	Canada	Cross-sectional; n = 466 (no control); non-occupational (food)/chronic	Female = 466 (20-54y)	High	Anemia = 200, normal = 266	Previous data not shown. Pearson r = 0.04, p-value not informed	3
Yildrim et al. [37] (2012)	Turkey	Case series; n = 5; non-occupational (home)/acute	Female = 3, male = 2 (20-54y)	High	Anemia = 2, leukopenia = 2, thrombocytopenia = 2, normal = 2	NA	3
Priya et al. [11] (2012)	India	Case report; n = 1; non-occupational (suicide)/acute	Female (19y)	High	Anemia = 1, leukopenia = 1, thrombocytopenia = 1	NA	3
Khoury et al. [104] (2013)	Brazil	Cross-sectional; n = 157 (exposed = 108, not exposed = 49); non-occupational (gold mining + food)/chronic	NI = 157 (13-53y)	Normal = 49, high = 108	NI	ND	3
Kim et al. [50] (2013)	Korea	Cross-sectional; n = 311 (no control); non-occupational (food)/chronic	Female = 141, male = 170 (5-12y)	High = 7	Lymphocytosis = 100, normal = 211	Spearman r = 0.121, p = 0.049	3
Wu et al. [72] (2013)	Taiwan	Case report; n = 1; non-occupational (medicine)/acute	Male (51y)	Normal	Anemia = 1	NA	3
Beasley et al. [105] (2014)	New Zealand	Case report; n = 1; non-occupational (suicide)/acute	Female (19y)	High	Leukocytosis = 1, neutrophilia = 1	NA	3
Brázdová et al. [47] (2014)	Kazakhstan, Kyrgyzstan, Uzbeskistan	Cross-sectional; n = 60; non-occupational (environment)/ chronic	Female = 27, male = 33 (1-15y)	Normal	Anemia = 60	Bonferroni's test, mean difference, p < 0.05	3
Dardamanis et al. [106] (2014)	Greece	Case report; n = 1; non-occupational (thermometer)/ acute	Female (48y)	NI	Anemia = 1	NA	3
Cicek-Senturk et al. [107] (2014)	Turkey	Case report; n = 3; non-occupational (home)/chronic	Female = 1, male = 2 (14y, 52y, NI)	High	Anemia = 1, leukocytosis = 3	NA	3
Mathee et al. [48] (2014)	South Africa	Cross-sectional; n = 307 (exposed = 60, not exposed = 247); non-occupational (geophagia)/chronic	Female = 307 (18-46y)	Normal	Anemia = 52, normal = 255	No association (OR not informed), no mean difference, p = 0.183	2
Kim et al. [51] (2015)	Korea	Cohort; n = 4,350 (no control); non-occupational (food)/ chronic	Female = 2,175, male = 2,175 (7y)	High	Basophilia = 191, neutrophilia = 191, lymphopenia = 191, normal = 4,159	Linear mixed model, β = 1.38 (95%CI: 0.11; 2.65)	2

(continues)

Table 2 (continued)

Study (year)	Country	Study characteristics [design/number/exposure]	Population [age/sex]	Mercury level	Hemtologic effect	Statistical analysis	EPHPP tool
Oulhote et al. [52] (2017)	Denmark	Cohort; n = 56 (no control); non-occupational (food)/ chronic	Female = 33, male = 22, NI = 1 (7-12y)	Normal, high *	Leukopenia = 56, basopenia = 56, lymphopenia = 56, monocytopenia = 56	Structural equation, β = -0.23 (95%CI: -043; -0.04), p = 0.02	2
Weinhouse et al. [53] (2017)	Peru	Cross-sectional; n = 83 (no control); non-occupational (gold mining + food)/chronic	Female = 44, male = 38, NI = 1 (< 12y)	Normal = 35, high = 48	Anemia = 41, normal = 42	Multivariate linear, regression model, β = -0.14g/dL, p = 0.04	2

95%CI: 95% confidence interval; EPHPP: Effective Public Health Practice Project; NA: not applicable; ND: not done; NI: not informed.

* From normal to high levels of mercury (range).

It is important to emphasize the growing articles publication involving human exposure to chemical substances over the past decades. This is a consequence of the efforts made by many countries, through their agencies and institutions, in order to improve health by reducing environmental exposure to toxic substances [55,56]. Mercury is no exception, as in this review, we reported 26 studies published between the 1950s and the 1980s and 54 studies in the last three decades [57].

Distribution by age and sex presented the results expected in the literature, where children/teenagers and women were more commonly exposed non-occupationally, while adults and men were occupationally exposed. According to the report on human exposure to environmental chemicals (*National Health and Nutrition Examination Survey IV* – NHANES), women are the most exposed on non-occupational setting [8]. The main exposure pathway for children/teenagers was food consumption, mainly fish and shellfish, although rice may be another methylmercury source for Asians [58]. Another concern regarding this group is the fact that this silver liquid metal – found at home, at school and at others sites where it is not adequately stored – is seen by them as an amusing substance to play with, which may cause health problems. Lee et al. [59] addressed this subject by reviewing the sources of mercury exposures in children, the location and proportion of children affected and also making recommendations to prevent them.

There was a wide range of exposure pathway, from food and medicine intake, suicide attempt to industrial process and gold mining, among others. Many of them are supposed to be prohibited by 2020, according to *Minamata Convention*, an international treaty signed in 2013 by more than 140 countries, including Brazil, which have committed to eliminate the use of mercury in different products, such as batteries, light bulbs and health equipment [2]. Two of them deserve a special attention: gold mining/ASGM and fish/shellfish consumption, since they play a role in both types of exposure, occupational and non-occupational.

The first exposure pathway, gold mining/ASGM, is the main anthropogenic mercury pollutant in the world, affecting not only the miners but also the neighboring population, mainly in Southeast/East Asia, Sub-Saharan and South America [2]. It is impressive that only seven research articles (four occupational and three non-occupational) have addressed hematological effects among people working or living nearby the gold mining sector, as more than 10 million ASGM miners, most of them informally or even illegally [5], are exposed to mercury through both direct inhalation of mercury vapor and consumption of material taken from contaminated areas (e.g. fish). One example addressing this topic was the research, a purposive field sampling, conducted in Indonesia by Ekawanti & Krisnayanti [60] among non-miners (29) and miners (71), who showed lower levels of hemoglobin and hematocrit. In non-occupational situations, houses near gold mining put the surrounding population at risk due

Table 3

Mercury's occupational exposure studies.

Study (year)	Country	Study characteristics [design/number/exposure]	Population [age/sex]	Mercury level	Hemtologic effect	Statistical analysis	EPHHP tool
Butt & Simonsen [41] (1950)	USA	Cross-sectional; n = 134, no control (occupational = 1, non-occupational = 55, NI = 78); occupational (fur cleaning plant)/chronic	Female (49y)	High	Thrombocytopenia = 1	ND	3
Devlin & Sudlow [108] (1967)	UK	Case report; n = 1; occupational (laboratory)/chronic	Male (32y)	High	Leukopenia = 1, thrombocytopenia = 1	NA	3
Takamatsu et al. [109] (1969)	Japan	Case series; n = 5; occupational (agriculture)/chronic	Male = 5 (adults = 5)	High = 5	Leukopenia = 5	NA	3
Ryrie et al. [38] (1970)	UK	Case report; n = 1; occupational (thermometer fabric)/acute	Male (59y)	High	Anemia = 1, leukopenia = 1, thrombocytopenia = 1	NA	3
Gys & Fadeev [80] (1971)	USSR	Cross-sectional; n = 103 (no control); occupational (agriculture)/chronic	NI (adults = 103)	ND	Leukopenia = ?	ND	3
Nizov & Shestakov [110] (1971)	USSR	Case series; n = 10; occupational (agriculture)/acute	NI (adults = 10)	ND	Anemia = 10, leukopenia = 10	NA	3
Jung & Aaronson [111] (1980)	USA	Case report; n = 1; occupational (gold mining)/acute	Male (53y)	High	Polycythemia = 1; leukocytosis = 1; neutrophilia = 1	NA	3
Lien et al. [86] (1983)	Canada	Case series; n = 7 (occupational = 1, non-occupational = 6); occupational (gold mining)/acute	Male = 1 (28y)	High = 1	Leukocytosis = 1	NA	3
Kanamaru et al. [75] (1984)	Japan	Cross-sectional; n = 1,164 (no control); occupational (agriculture)/chronic	Female = 397, male = 767 (adults = 1,164)	Female x = 2.97, male x = 5.35	Anemia = 197, normal = 967	ND	3
Langworth et al. [44] (1993)	Sweden	Cross-sectional; n = 110 (exposed = 71, not exposed = 39); occupational (chlor-alkali fabric/lamp facgtory/dentist office)/chronic	Female 75, male = 35 (exposed x = 49y, not exposed x = 40y)	Exposed x = 4.3, not exposed x = 3.9	Normal = 110	t-test, no mean difference, Pearson r not informed, no correlation	3
Torresani et al. [112] (1993)	Italy	Case report; n = 1; occupational (agriculture)/chronic	Female (54y)	ND	Eosinophilia = 1	NA	3
Zavariz & Glina [13] (1993)	Brazil	Cross-sectional; n = 91 (no control); occupational (lamp fabric)/chronic	Female = 8, male = 83 (20-65y)	High = 54, normal = 32, NI = 42	Anemia = 1, leukopenia = 6, lymphocytosis = 6, eosinophilia = 5, neutrophilia = 4, normal = 69	ND	3

(continues)

Table 3 (continued)

Study (year)	Country	Study characteristics [design/number/exposure]	Population [age/sex]	Mercury level	Hemtologic effect	Statistical analysis	EPHHP tool
Moszczyński & Slowiński [22] (1994)	Poland	Cross-sectional; n = 91 (exposed = 55, not exposed = 36); occupational (chlor-alkali fabric)/chronic	Male = 91 (28-55y)	High = 55, normal = 36	Lymphocytosis = 55, normal = 36	t-test, no mean difference, Pearson r = 0.3405, p < 0.05	3
Alvarado et al. [34] (1995)	Costa Rica	Case report; n = 2 (occupational = 1, non-occupational = 1); occupational (compressor)/chronic	Male (30y)	High	Normal = 1	NA	3
Moszczyński et al. [23] (1995)	Poland	Cross-sectional; n = 117 (exposed = 81, not exposed = 36); occupational (chlor-alkali fabric)/chronic	Male = 117 (21-60y)	Exposed x = 54	Lymphocytosis = 81, normal = 36	t-test, no mean difference, Pearson r = -0.11, 0.10, no correlation	3
Queiroz & Dantas [12] (1997)	Brazil	Cross-sectional; n = 41 (exposed = 33, not exposed = 8); occupational (chlor-alkali fabric)/chronic	NI (19-46y)	Normal = 41	Lymphopenia = 33, normal = 8	Mann-Whitney's U, mean difference, p < 0.05, Pearson r = -0.077, no correlation	3
Melo et al. [113] (2000)	Venezuela	Cross-sectional; n = 47 (no control); occupational (dentist office)/chronic	NI	NI	Hemoglobin alteration = 4, leukocyte alteration = 3, normal = 40	ND	3
Zabiński et al. [45] (2000)	Poland	Cross-sectional; n = 81 (exposed = 46, not exposed = 35); occupational (chlor-alkali fabric)/chronic	NI (20-56y)	x = 77.44 ± 48.15 (exposed/not exposed)	Polycythemia = 46, normal = 35	t-test, mean difference, 47.89% vs. 46.1%, p < 0.05	3
Soleo et al. [24] (2002)	Italy	Cross-sectional; n = 289 (exposed = 117, not exposed = 172); occupational (lamp fabric)/chronic	NI (adults = 289)	Normal = 289	Lymphocytosis = 117, normal = 172	t-test, no mean difference, Pearson r = 0.184, positive correlation	3
Campbell et al. [74] (2009)	UK	Case report; n = 1; occupational (lamp fabric)/acute	Male (25y)	High	Polycythemia = 1	NA	3

(continues)

Table 3 (continued)

Study (year)	Country	Study characteristics [design/number/exposure]	Population [age/sex]	Mercury level	Hemtologic effect	Statistical analysis	EPHHP tool
Rodríguez et al. [114] (2002)	Spain	Cross-sectional; n = 26 (no control); occupational (gold mining)/chronic	NI	ND	Anemia = 26	NA	3
Alhamad et al. [115] (2011)	USA	Case report; n = 1; occupational (thermometer fabric)/acute	Male = (36y)	High	Leukocytosis = 1, eosinophilia = 1	NA	3
Douine et al. [54] (2018)	Guyana/ Suriname	Cross-sectional; n = 421 (exposed = 202, not exposed = 219); occupational (gold mining)/chronic	Female = 124, male = 297 (x = 37y)	ND	Anemia = 93, normal = 328	Prevalence 22% (95%CI: 18.0; 25.9)	2

95%CI: 95% confidence interval; EPHPP: Effective Public Health Practice Project; NA: not applicable; ND: not done; NI: not informed.

to contamination of soil (children playing outdoor), water (fish consumption) and air (amalgamation process or re-burning it at gold shops) [5]. An example of the latter was a study carried out in Poconé, a town in Mato Grosso State/Brazil [61]. They evaluated the levels of exposure to metallic mercury emissions by gold dealers and its health effects. It was reported higher mercury levels and referred morbidity among downtown residents.

The second route of exposure, consumption of fish and shellfish, is a major concern for regulatory agencies around the world, because although it is an important part of a healthy diet (presence of omega-3 fatty acids and low in saturated fat), it is also cited as the most significant source of methylmercury. One of the agencies is the U.S. Environmental Protective Agency (EPA), who sets a recommendation to limit or avoid certain species of fish and shellfish for general public and for specific groups of people at risk, such as: high consumers of fish (e.g. coastal dwellers, riverside communities), women of childbearing age, pregnant and breastfeeding women and young children. For example, the threshold for tuna consumption, a carnivorous fish, is one can (226-340g) per week for groups of people at risk [62]. The risk of contamination of this kind of food is usually high (especially for the species at the top of food chain), because of the bioavailability of this metal in the aquatic environment from different sources such as geothermal activities, fossil fuel burning, hazardous waste incineration, industrial processes, gold mining and so forth. The ASGM, despite its decline in Amazon Basin, continues to contribute to an increase in the mercury load, becoming a major risk for indigenous groups and riverside communities, who have fish as their main source of protein [63]. On other hand, the general urban population has a low fish ingestion as a result of its cultural and social characteristics, in such a way that they do not face significant health effects from this pathway exposure [64,65]. However, the fish resources for urban centers may come from a contaminated water body, as reported by Hacon et al. [64] in a study carried out in Alta Floresta, a town in Mato Grosso State/ Brazil. The assessment of the impact of fish and shellfish contamination on the exposure of human beings and on their health through food deserves special attention, specifically, but not only, for those who are large consumers, such as indigenous groups, riverside communities (e.g. Amazon Basin), coastal (e.g. Florida/Puerto Rico) and island dwellers (e.g. Faroe Islands/Denmark). In this review, 3 articles have targeted this population and hematological effects: 1 sectional study with an indigenous group from the Peruvian Amazon near ASGM, that reported anemia among children under 12 years (83 persons) [66]; 1 cohort with children from Faroe Islands (56 persons), that reported leukopenia and lymphopenia [52], and other sectional with children from Jeju Island/South Korea (311 persons), that reported lymphocytosis [50].

Anemia and less commonly leukopenia, eosinophilia, thrombocytopenia and pancytopenia have been reported due to mercury toxicity [67]. In this review, most exposed people (75.85%) had a normal

blood cell count, however, hematological effects were reported 2,376 times, mainly at non-occupational settings, comprising 1,914 cases. All bone marrow cellular series were affected and the most common, for both exposures, was the erythroid series with anemia (875). Out of five studies that addressed this subject using statistical analysis with significant p-value, there was mean difference in two [43,47], none in one study [42]; negative correlation [42] was reported in one and inverse association [53] in another. On the other hand, polycythemia was also reported in the mercury exposure group and a mean difference was found [45]. Other two hematological effects were also reported: lymphocytosis and lymphopenia. For the first outcome, there were three studies that reported a weak to moderate positive correlation [22,24,50] between lymphocytes and mercury. For the latter, one reported mean difference [12] and other two described inverse association between lymphocytes and mercury exposure [51,52]. One of these studies also described an association between mercury exposure and an increased neutrophils and basophils percentage [51]. These results confirm there are relation or association between mercury exposure and hematological effects, especially for anemia, lymphopenia, lymphocytosis, neutrophilia and basophilia. However, none of these studies could determine a causal relationship, as they were not designed for this purpose.

Recently, researches shed some light on the role of heavy metal exposure at anemia, which is estimated by the World Health Organization (WHO) in 1.62 billion cases (95%CI: 1.0; 1.74 billion) [47,48,49]. More than half of the cases are caused by iron deficit (51%) and current data point to relation between heavy metals, such as lead and mercury, and iron metabolism (positive correlation for mercury and inverse for lead) [49,68].

There is some scientific debate about mercury effect on lymphocytes. It is suggested that the difference observed (lymphopenia x lymphocytosis) could be explained by mercury's level and form, in a way those exposed to methylmercury would be prone to lymphopenia and those to metallic or inorganic mercury to lymphocytosis [50,52,69,70]. The latter effect on lymphocytes was observed in six out of seven studies, which might corroborate this theory.

Some hematological effects are considered quite severe according to preestablished criteria and can lead to a number of critical clinical conditions. They were seen at this review as a consequence of mercury's direct effect on blood cell and their corresponding clinical pictures, mainly as severe bleeding, but also as renal insufficiency, multiple organ dysfunction syndrome and sepsis. Despite the reports of other potential severe hematological effects, such as polycythemia, thrombocytosis and lymphocytosis, there were no cases of thrombosis or hematological cancer.

Mercury is a toxic substance that can lead to death. Its lethal dose is defined at 150 to 300mg/70kg [6]. There were 29 reports of it mainly on non-occupational exposure, especially due to use of medicine in a chronic way. In the past it was prescribed as laxative, diuretic and antiseptic. Nowadays, mercury is still present in some traditional therapies and religious practices (e.g. *Santería*, *Espiritismo* or Ayurvedic medicine) [71,72] as well as in vaccine preservative. All the five occupational deaths were related to higher level of mercury exposure at acute setting.

There are some explanations for some mercury hematological effects, such as: pancytopenia due to direct toxic effect on bone marrow [11,67]; anemia due to apoptosis [14,15], loss of blood from direct effect on gastrointestinal mucosa [73] and hemolysis [14,15,36]; polycythemia from increased level of erythropoietin [45,74]; leukopenia, neutropenia, lymphopenia and basopenia due to passed inflammatory reaction [46] and apoptosis [69,70]; leukocytosis and neutrophilia due to lung inflammatory reaction (pneumonitis) [75,76]; eosinophilia related to hypersensitivity [77,78] and idiosyncrasy [79]; lymphocytosis due to increased calcium content in cytoplasm [23], and; thrombocytopenia immunologically mediated [39,80].

The actual dimension of mercury's hematologic effects is unknown for many reasons that come from the lack of studies that could evaluate this topic as a primary goal, which was discussed by two studies [39,81] to the lack of knowledge of mercury role on this subject. In the latter, two situations were observed: the physician did not request mercury biomarker when evaluating an hematological effect or he did not request blood cell count when evaluating a case of mercury intoxication, merely because of the lack of knowledge. In this review, only 14 studies had hematological effect as main outcome of mercury exposure and 381 out of 1,158 studies were excluded due to the fact of not requesting blood cell count.

A meta-analysis was not pursued because the only hematological effect that had a sufficient number of comparable groups and a statistical measure (correlation coefficient *r*) was lymphocytes

alteration (lymphocytosis or lymphopenia). There were differences in reporting this measure: one study did not report the *r* value and four, its statistical significance.

We have tried to mitigate the publication bias by a comprehensive, sensitive, unrestricted search for language, with a long period of time (more than 70 years) and search in the gray literature (e.g. congress, master and thesis). We were able to retrieve a significant amount of normal blood cell count results between exposed people as a consequence of a more sensitive search that included blood cell count as a key term. As a meta-analysis was not done, both the visual evaluation of the funnel plot and the statistical tests of hypothesis were not performed.

The quality assessment of these studies was considered weak according to EPHPP, a quality assessment tool (global ratings: 3) for 75 studies out of 80. This poor quality of most studies, mainly due to the study design, absence of possible confounders' evaluation and presence of bias risk, limited the power of the epidemiological studies included. However, these data were able to identify, in absolute terms, 20% of hematological effects on the presence of mercury exposure, in particular for anemia, lymphopenia, neutrophilia and basophilia, as statistical tools with significant p-value were used. Without any doubt, this should stimulate further researches with special attention to studies of methodological elaboration. All steps of this process must be thoroughly thought, including random selection, comparison between exposure and non-exposure groups, control for confounders according to bone marrow cell affected (e.g. micronutrients, enteroparasitosis, malaria, others infections, glutathione S transferase deletion polymorphisms) and data collection methods that should be reliable and valid. For obvious ethical reasons, no clinical trials will be conducted to study this potential association. However, there are some others observational studies that can be done aiming, for example the frequency of this outcome (cross-sectional with comparing groups; case-control; multicentric cohort studies), the risk assessment of this exposure, as well to ascertain the clinical significance of this relationship.

Conclusion

This review was able to retrieve a significant number of studies for an issue with sparse information, although only few of them have evaluated hematological effect as the primary outcome. Despite the fact that the majority of exposed individuals had normal blood cell count and mercury hematological effects do not seem very usual, few studies reported association from refined observational study designs including robust statistical analysis, especially for anemia, lymphopenia, neutrophilia and basophilia. In this way, the effects of mercury on health should receive worldwide attention because of its toxicity and wide source of human exposure. Researchers, as well as health practitioners, should be aware of the potential hematological effect as sometimes it can be severe and even lethal.

Contributors

A. S. Vianna, E. P. Matos, and C. I. R. F. Asmus contributed in the elaboration of study and search terms, assessment of the articles reviewed, and article writing. I. M. Jesus contributed in the elaboration of study and article writing. V. M. Câmara contributed in the elaboration of study and search terms, discussion of results, and article writing.

Additional informations

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Resumo

O mercúrio é um metal que pode ser encontrado naturalmente no meio ambiente e através de fontes antropogênicas. É altamente tóxico para ecossistemas e seres vivos. A maior parte da exposição humana provém da ingestão de pescados contaminados, da liberação de gases da amálgama dentária ou da exposição ocupacional (p.ex.: extração de ouro). Vastas populações são expostas ao mercúrio, tornando-se uma questão de saúde pública muito importante. Efeitos adversos à saúde são comumente observados no sistema nervoso, mas todos os órgãos são alvos em potencial, como a medula óssea. O principal objetivo do estudo foi avaliar as evidências disponíveis sobre a exposição humana ao mercúrio e seus efeitos hematológicos. Uma estratégia de busca foi realizada, incluindo termos chave (palavras-chave, palavras do texto e equivalentes), para pesquisar dois repositórios de dissertações de mestrado e teses de doutorado (Fiocruz/ARCA e Universidade de São Paulo) e quatro bases de dados eletrônicas: BVS/LILACS, MEDLINE/PubMed, Scopus e TOXLINE/NIH (artigos publicados de 1950 até fevereiro de 2018). Não houve restrições de linguagem e uma ferramenta (EPHPP) foi utilizada para avaliar a qualidade dos estudos incluídos. De acordo com os critérios pré-estabelecidos, foram encontrados 80 estudos, todos observacionais (48 relatos de caso, 24 estudos transversais, 6 séries de casos e 2 coortes), que compreendiam 9.284 pessoas. Apesar do fato de que as pessoas mais expostas (6.012) tinham contagens de células sanguíneas normais, e os efeitos hematológicos do mercúrio não pareciam muito comuns (1.914 casos, 14 graves e 29 mortes), três estudos relataram a associação de (β) anemia, linfopenia, neutrofilia e basofilia. Concluímos que as informações coletadas indicam efeitos hematotóxicos do mercúrio, alguns dos quais podem ser muito graves e até fatais.

Intoxicação por Mercúrio; Intoxicação por Metais Pesados; Mercúrio; Contagem de Células Sanguíneas

Resumen

El mercurio es un metal que se puede encontrar de forma natural en el ambiente y mediante fuentes antropogénicas. Es altamente tóxico para los ecosistemas y seres vivos. Entre otras, la mayor parte de la exposición humana, proviene de la ingestión de pescado contaminado, liberación de gases de amalgamas dentales o exposición ocupacional (p.ej. extracción de oro). Vastas poblaciones están expuestas al mercurio, convirtiéndolo en un asunto muy importante desde la perspectiva de la salud pública. Los efectos adversos para la salud se observan comúnmente en el sistema nervioso, pero cada órgano es un objetivo potencial, como la médula ósea. El objetivo principal del estudio fue evaluar las evidencias disponibles sobre la exposición humana al mercurio y sus efectos hematológicos. Se realizó una estrategia de búsqueda, incluyendo términos clave (palabras-clave, palabras del texto y equivalentes), se consultaron 2 registros de trabajos finales de máster y tesis de doctorado (Fiocruz/ARCA y Universidad de São Paulo) y 4 bases de datos electrónicas diferentes: BVS/LILACS, MEDLINE/PubMed, Scopus y TOXLINE/NIH, para artículos publicados desde el año 1950, hasta febrero de 2018. No hubo restricciones de lengua y se usó la herramienta (EPHPP) para evaluar la calidad de los estudios incluidos. De acuerdo con los criterios preestablecidos, se recopilaron 80 estudios, todos observacionales (48 informes de casos, 24 estudios transversales, 6 series de casos, y 2 cohortes), que comprendieron a 9.284 personas. A pesar de que la mayoría de los expuestos (6.012) tenían un recuento normal de células sanguíneas y los efectos hematológicos del mercurio no parecían muy comunes (1.914 casos: 14 severos y 29 muertes), tres estudios informaron de la asociación (β) para anemia, linfopenia, neutrofilia y basofilia. Concluimos que la información recabada indicaba los efectos hematotóxicos del mercurio, algunos de los cuales pueden ser muy serios e incluso fatales.

Intoxicación por Mercurio; Intoxicación por Metales Pesados; Mercurio; Recuento de Células Sanguíneas

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