SIGNS AND SYMPTOMS OF MERCURY-EXPOSED GOLD MINERS

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Abstract
Objectives: Gold miners use mercury to extract gold from ore adding liquid mercury to the milled gold-containing ore. This results in a mercury-gold compound, called amalgam. Miners smelt this amalgam to obtain gold, vaporizing it and finally inhaling the toxic mercury fumes. The objective was to merge and analyze data from different projects, to identify typical signs and symptoms of chronic inorganic mercury exposure. **Material and Methods:** Miners and community members from various artisanal small-scale gold mining areas had been examined (Philippines, Mongolia, Tanzania, Zimbabwe, Indonesia). Data of several health assessments were pooled. Urine, blood and hair samples were analyzed for mercury (N = 1252). Questionnaires, standardized medical examinations and neuropsychological tests were used. Participants were grouped into: Controls (N = 209), living in an exposed area (N = 408), working with mercury as panners (N = 181), working with mercury as amalgam burners (N = 454). Chi² test, linear trend test, Mann-Whitney test, Kruskal-Wallis test, correlation coefficient, Spearman's rho, and analysis of variance tests were used. An algorithm was used to define participants with chronic mercury intoxication. **Results:** Mean mercury concentrations in all exposed subgroups were elevated and above threshold limits, with amalgam burners showing highest levels. Typical symptoms of chronic metallic mercury intoxication were tremor, ataxia, coordination problems, excessive salivation and metallic taste. Participants from the exposed groups showed poorer results in different neuropsychological tests in comparison to the control group. Fifty-four percent of the high-exposed group (amalgam burners) were diagnosed as being mercury-intoxicated, compared to 0% within the control group (Chi² p < 0.001). **Conclusions:** Chronic mercury intoxication, with tremor, ataxia and other neurological symptoms together with a raised body burden of mercury was clinically diagnosed in exposed people in artisanal small-scale mining areas. The mercury exposure needs to be urgently reduced. Health care systems need to be prepared for this emerging problem of chronic mercury intoxication among exposed people. Int J Occup Med Environ Health 2017;30(2):249–269

INTRODUCTION

Artisanal and small-scale gold mining (ASGM) often relies on mercury (Hg) to extract gold. Miners obtain the gold-containing ores either from underground or from open pit deposits. In order to free the gold particles, it is sometimes necessary to grind the ore mechanically to a fine powder using, e.g., ball mills. The powder is further processed, adding liquid mercury, with or without pre-concentration. Miners are panning this mixture of fine powder, liquid mercury and water, during this so-called "amalgamation," the fine gold particles bind to mercury, resulting in a mercury-gold compound, called "amalgam." To obtain the gold from the amalgam, it is heated until the mercury evaporates, and after this smelting a piece of raw gold sponge remains. This last step is performed by the so called "amalgam burners" or smelters. At both stages (amalgamation and smelting) miners are exposed to mercury, in the case of:

– amalgamation (or panning) – liquid elemental mercury via skin contact and via inhaling evaporating mercury,
– smelting – elemental mercury vaporization via inhalation,
– storing mercury at home – elemental mercury evaporation via inhalation.

The main exposure of these miners is therefore to elemental mercury. Mercury shows acute and chronic toxicity which may result in severe neurological damage affecting especially the cerebellum [1,2]. The described practice of ASGM is very common; it is estimated that up to 10–15 million miners work in ASGM areas [3–5]. The chronic exposure to elemental mercury vapor causes health problems among the miners and the people in the mining communities [6–33]. Most of these publications focused on mercury concentration in human samples, only few studies included physical examinations of miners and revealed relevant symptoms [26,31–33]. In our own ASGM studies we had examined a large numbers of miners clinically (Table 1) [17–20,34–37]. The focus was on subjective and objective symptoms of mercury intoxication among miners (smelters and panners) and people living in mining areas compared to a non-exposed control group living outside mining areas.

The intention for this publication was to merge and analyze the data from the different projects, to identify the most typical signs and symptoms of chronic exposure to inorganic mercury.

Table 1. Data sources for the analysis of signs and symptoms of mercury-exposed gold miners

Country, area	Year of the study	Study design	Main outcome	Project partners	References
Indonesia					
Kalimantan	2003	miners, males and females, children; mining community from Galangan; no control group	"Hg-exposed workers showed ataxia, tremor, dysdiadochokinesia. [...] The Hg concentration in the biomonitors was high. [...] Diagnosis of chronic Hg intoxication was made for highly burdened workers (amalgam burners) in 55% in Sulawesi and in 62% in Kalimantan" [15].	CETEM, LMU, UNIDO	15, 56, 65
Sulawesi	2003	miners, males and females, children; mining community from Talawaan; control group from Air Mandidi		CETEM, LMU, UNIDO	15, 56, 65
Mongolia	2008	women at child bearing age; mining communities Bornuur sum, Jargalant sum; control group from Khushaat sum	"The body burden resulting from the use of Hg in artisanal gold mining is high not only in the miners themselves, an increased Hg hazard was also found for inhabitants of mining areas who were not actively involved in mining" [18].	MoH, LMU, UMIT, WHO	18, 66
Philippines	1999	miners, males and females, children; mining community from Mt. Diwata and Monkayo; control group from Davao	"0% of the controls, 38% downstream, 27% from Mt. Diwata, non-occupational exposed and 71.6% of the workers were classified as Hg-intoxicated" [17].	BGS, LMU, UNIDO	17, 67, 68
Tanzania	2003	miners, males and females, children; mining community from Rwamagasa; control group from Katoro	"104 amalgam-burners, the most exposed population group, were examined. 25 of these workers were found to be intoxicated. Small-scale mining is a serious health hazard for amalgam burners" [16].	BGS, LMU, UNIDO	16, 69, 70
Zimbabwe	2004	miners, males and females, children; mining community Kadoma; control group from Chikwaka	"Raised Hg levels in the urine, blood and hair. Symptoms of severe damage of the brain (cerebellum) such as ataxia, tremor and movement disorders were found in the mining communities. In 70% of the amalgam burners in Kadoma a Hg intoxication was diagnosed" [37].	BRGM, LMU, UNIDO	37, 71, 72
	2006	women at child bearing age and their breast fed infants; mining community Kadoma; control group from Chikwaka	"120 breast milk samples were analyzed, median levels were (i) control group < 0.50 [μg/l], (ii) medium-exposed group 1.10 Hg [μg/l], (iii) high-exposed group 1.20 Hg [μg/l] (p = 0,000). No infant from the control group, but 17.6% of the medium- and 18.5% of the high-exposed group were above the reference dose" [71].	LMU, UoZ	31, 71

CETEM (Centro de Tecnologia Mineral) – Brazilian Centre for Mineral Technology; LMU – Ludwig-Maximilians University Munich, Germany; UNIDO – United Nations Industrial Development Organization; MoH – Mongolian Ministry of Health; UMIT (Private Universität für Gesundheitswissenschaften, Medizinische Informatik und Technik) – The Health and Life Sciences University, Hall, Austria; WHO – World Health Organization; BGS – British Geological Survey; BRGM (Bureau de Recherches Géologiques et Minières) – Geological and Mining Research Bureau; UoZ – University of Zimbabwe.

MATERIAL AND METHODS

This study shows the analysis of merged data from several cross-sectional studies.

Data sources

Data from former projects were used for this analysis (Table 1). A data bank including all our project data was created and used for this analysis [16].

Data from different projects were pooled: from the Global Mercury Project (GMP) data from the Philippines, Indonesia, Zimbabwe and Tanzania; from World Health Organization (WHO) projects data from Mongolia and from a university project Ludwig-Maximilians University Munich, Germany (LMU) data from Zimbabwe in 2006. For this analysis we selected data from adult miners (18–60 years of age).

The results for children had already been published [38].

Thirty-three participants with known severe neurological diseases such as a stroke or Parkinson's disease, and participants obviously drunk during examination were excluded from this analysis. Besides, only participants with reliable exposure history were included, while former miners and miners who had moved to a control area were left out of this analysis. For the project in Kalimantan, Indonesia, we could not use the data of the control group. The laboratory results showed that this group was in fact also an exposed group of miners. In total, 1252 participants were available for further analysis.

The data was stratified according to the different level of exposure:

1. Non-exposed group – control groups, outside of ASGM areas, with no specific contact to mercury (N = 209). Control groups were selected by the national project manager, trying to match to comparable social and economic backgrounds to exposed groups.
2. Low-exposed group – living in exposed areas, but not engaged in mining activities related to mercury (N = 408).
3. Medium-exposed group – working with mercury as panners (N = 181).
4. High-exposed group – working with mercury as amalgam burners (N = 454).

All participants were volunteers. The national project manager together with the respective local health experts selected the participants, according to the inclusion criteria of the specific project. The criteria were: age group, gender and exposure status – the aim was to have sufficient participants within each subgroup. According to these criteria, local study nurses went to their villages and recruited volunteers that fulfilled these criteria. In our opinion, this was the best feasible way in ASGM areas to select participants.

It was not possible in all the field projects to have exactly the same study protocol. For Indonesia, Tanzania and Zimbabwe 2004 the data set was the most complete, including, e.g., speciation of the hair samples. Fewer data parameters were available mainly for Mongolia and Zimbabwe 2006.

For each single project, the involved international institutions (United Nations Industrial Development Organization – UNIDO, United Nations Development Programme – UNDP, WHO) had provided the approval of the relevant national committees to perform the health assessments. Written informed consent in the appropriate regional language was achieved from all volunteering participants. All assessments were carried out respecting the Recommendation for Conduct of Clinical Research from World Health Organization Declaration of Helsinki. The health examinations were performed in close cooperation with UNIDO (United Nations Industrial Development Organization), the United Nations Development Programme (UNDP), WHO, as well as the regional health authorities and national ministries of health. Extensive legal, formal, and ethical issues were considered and all conditions were agreed upon between the governments and WHO/UNIDO. These conditions, approved by the governments, complied with all relevant national, state, and local regulations.

Health assessment

An extensive questionnaire, translated into the regional language was applied by local nurses to get information on exposure data, possible confounders such as fish intake or alcohol ingestion, health data including typical symptoms of mercury toxicity such as memory problems, sleeping disturbances, headache, metallic taste or excessive salivation. The participants were clinically, mainly neurologically examined by the same examiner (S.B.), who was blinded for mercury levels of participants. Ataxia, tremor, coordination problems, abnormal reflexes and grey to bluish discoloration of the oral cavity, number of dental amalgam fillings were the main items of the examination, all related to chronic mercury exposure. The signs and symptoms were scored and, if appropriate, Masur's Scales and Scores in Neurology were used [39].

To assess the physical and mental fatigue, a special score was used [40]. The physical score, ranging 0–16, takes into account personal complaints, e.g., need to rest more, getting tired easily, feeling sleepy, lack of energy, less strength in muscles, feeling weak. The mental score, ranging 0–10, consists of problems to concentrate, thinking clearly and problems with memory. Several neuropsychological and neuromotor tests were performed to assess memory, tremor, ataxia and coordination. The following neuropsychological and neuromotor tests were carried out [39,41,42]:

– digit span test to test the short-term memory (part of Wechsler Memory Scale) – the more numbers in a row a participant can recall without a mistake the better,
– matchbox test to test for coordination, intention tremor and concentration – 20 matches are outside an empty matchbox 15 cm away to both sides and the faster a participant can put the matches back in the box the better,
– Frostig score (subtest Ia 1–9) to test for tremor and visual-motoric capacities – drawing a line with a pencil between 2 given lines, the lines should not be touched or crossed,
– pencil tapping test to test for intention tremor and coordination – tapping with a pencil within 10 s dots on a piece of paper, the more dots the better.

Laboratory analysis of urine, blood and hair

Urine, blood and hair samples were collected from the participants. Hair samples were cut from up to 3 cm from the scalp. Urine was acidified to avoid degradation. Blood was sampled in ethylenediaminetetraacetic acid (EDTA)-coated vials. Blood and urine were stored and transported at 4°C until the samples were analyzed. The analysis of the samples was in general performed in the Institute of Forensic Medicine (LMU): Blood, urine and hair were analyzed by G.R. and her team from LMU with a Cold-Vapor Atomic-Absorption Spectrometer (Perkin-Elmer 1100 B spectrometer and Lumex mercury Cold-Vapor Atomic-Absorption Spectrometer). To correct for urinary excretion, urinary mercury levels were adjusted for creatinine [43]. Hair samples were not washed, but pretreated and digested.

The urine and hair analysis for the controls from Mongolia was performed by the National Institute for Minamata Disease (Minamata, Kumamoto, Japan) using a Cold-Vapor Atomic-Absorption Spectrometer (CV-AAS) [20]. The blood analysis of the controls in Mongolia was performed by the Health and Safety Laboratory (Harpur Hill, Buxton, United Kingdom) using an Inductively-Coupled-Plasma Mass Spectrometer (ICP-MS).

Adequate strict external and internal quality control was guaranteed. Quality controls with reference samples were continuously achieved to guarantee the precision of the results. An extensive article on the results of our human biomonitoring data has been already published, and this article contains more detailed information on the laboratory methods [16] as well as our former country-related articles [17–20,44].

The limit of detection (LOD) for urine analysis was 0.1 μg/l for the controls from Mongolia, 0.2 μg/l for

Indonesia, Tanzania, Zimbabwe plus the exposed groups from Mongolia, 0.5 µg/l for the Philippines. The LOD for blood analysis was 0.2 µg/l for all countries, except for the Philippines with 0.50 µg/l. The LOD for hair analysis was 0.01 µg/g for the controls from Mongolia plus the Philippines, and 0.02 µg/g for Zimbabwe, Tanzania and Indonesia. For inorganic hair the LOD was 0.05 µg/g. For results below the limit of detection (LOD), the value was set to 1/2 the detection limit for the statistical analysis.

Mercury can damage the kidney function, and proteinuria is one of the consequences. With commercial kit (Bayer®) we tested for proteinuria.

Statistical methods

The analytic strategy was to describe signs, symptoms and mercury levels stratified by exposure group. Many test results were primarily scored and later reduced to a yes/no decision without loss of relevant information (score 1/0). The neuropsychological tests (memory, matchbox, Frostig, pencil tapping) were divided into 3 categories: best performing 25%, performing between 25% and 75% and worst performing 25% of participants (score 0/1/2).

The mercury concentrations in urine, blood and hair had a distribution with a tail to the right, and were therefore log-transformed. Descriptive measures (mean, median, range, standard deviation (SD), quartiles, 95% confidence limits, boxplots) were used. Metric human specimen data and neuropsychological data were analyzed using the Mann-Whitney test to search for differences between the groups and the Kruskal Wallis test to identify differences over all groups. Pearson's Chi^2 test was used to compare non-metric clinical data to see if there was any difference between the subgroups. To identify possible trends between the 4 groups (control, low-exposed, medium-exposed, high-exposed) the linear trend test was applied. To compare normal-distributed metric

data between subgroups, analysis of variance (ANOVA) was used. Univariate correlation of mercury levels with each other (nonparametric and parametric) and other parameters was applied (correlation coefficient and p-values by non-parametric Spearman's rho). Mercury levels were compared with recommended threshold values. The significance level has been set at $\alpha = 0.05$. The IBM SPSS version 20 software was used for the analysis.

Chronic alcohol ingestion causes severe neurological symptoms, such as tremor, depending on the dose and duration. Men are more likely to consume alcohol. A separate analysis for female/male participants of the 4 subgroups was performed to detect differences between the men and women [45]. Dental amalgam fillings contain elemental mercury, and might contribute to the body burden of mercury. The number of dental amalgam fillings was counted in the mouth of all participants. The objective of this study was to focus on the clinical signs and symptoms. The study was restricted to a univariate analysis of the data.

Fish contains methyl-mercury and contributes to the body burden of mercury. A correlation test was performed to test for a correlation between fish consumption and mercury levels in human specimens or medical score sum.

Threshold values and diagnostic algorithm

A medical score sum was formed, using anamnestic data, clinical data, neuropsychological parameters and the result of analyzing protein content in urine (Table 2). This medical score is based on the results from the first project in an ASGM area in the Philippines [19]. A high medical score sum is associated with the typical severe signs and symptoms of chronic mercury intoxication. The score ranged 0–21, a medical score sum 0–4 was considered as low, 5–9 medium and 10–21 high.

To stratify the health risk, we used the so-called human biomonitoring (HBM) values published by the German

Table 2. Medical score sum parameters in the study of signs and symptoms of mercury-exposed gold miners

Test	Score* [pts]
Anamnestic data	
metallic taste	0/1
excessive salivation	0/1
tremor at work	0/1
sleeping problems at night	0/1
health problems worsened since Hg exposed	0/1
Clinical data	
grey to bluish discoloration of the oral cavity	0/1
ataxia of gait	0/1
finger to nose tremor	0/1
dysdiadochokinesia	0/1
heel to knee ataxia	0/1
heel to knee tremor	0/1
mento-labial reflex	0/1
proteinuria	0/1
Neuropsychological tests	
memory test	0/1/2
matchbox test	0/1/2
Frostig test	0/1/2
pencil tapping test	0/1/2
Maximum	21

* Medical score sum parameters: anamnestic and clinical data: 0 – no symptom, 1 – pathological symptom; neuropsychological and neurometric tests: 0 – best quartile, 1 – 2nd and 3rd quartile, 2 – worst quartile [19].

Human Biomonitoring Commission [46,47]. The selection of threshold values applied for this study was discussed in our former papers [16,19,48]. The HBM values were recently updated, including the reference values [49]. Values < HBM I are considered as safe levels, between HBM I and II – as alert levels, and above HBM II – as action levels. Another threshold value is the biological tolerance value (BAT) from the German Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area. Workers with specimen levels above the BAT are not allowed to work any longer. For total mercury in hair, comparable limits were set [19].

The following categories were established (Table 3):
– below HBM I (if all specimens results were below HBM I),
– from HBM I to HBM II (if a least 1 specimen result was above HBM I but all below HBM II),
– from HBM II to BAT (if at least 1 specimen result was above HBM II but all below BAT) and, if available,
– above BAT (if any specimen result was above BAT).

To define a chronic mercury intoxication, an algorithm including the medical score and mercury threshold values in urine, blood and hair was developed using the results from our first study in the Philippines [19] (Table 4).

Table 3. Toxicologically established threshold limits for mercury in blood, urine and hair

Threshold/reference value	Mercury (Hg) threshold limit			
	urine		blood [µg/l]	hair [µg/g]
	µg/l	µg/g creatinine		
Reference value for adults	1.0	–	2.0	–
HBM				
< HBM I (low level)	≤ 7	≤ 5	≤ 5	≤ 1*
HBM I – HMB II (alert level)	> 7 to ≤ 25	> 5 to ≤ 20	> 5 to ≤ 15	> 1 to ≤ 5*
> HBM II (high level)	> 25	> 20	> 15	> 5*
BAT	> 30	> 25	> 25 (inorganic Hg)	–

* For hair there is no direct HBM level. The given values are derived from a stable ration between blood and hair [19].
HBM – Human Biomonitoring value; BAT – Biological Tolerance Values.

Table 4. Algorithm for the diagnosis of chronic mercury intoxication

Mercury presence	Medical score sum [pts]		
	0–4	5–9	10–21
In all specimens			
< HBM I	–	–	–
At least in 1 specimen			
> HBM I	–	–	+
> HBM II	–	+	+
> BAT	+	+	+

Abbreviations as in Table 3.
"–" – no intoxication, "+" – intoxication.

RESULTS

In most subgroups there were more female than male participants. Only the subgroup of medium-exposed participants was nearly equally distributed (Table 5). This needed to be considered in the further analysis, as it is likely that men had a higher exposure to mercury compared to women. The age of the 4 subgroups was comparable (30–32 years).

Table 5. Basic information about respondents in the study of signs and symptoms of mercury-exposed gold miners

Respondents characteristic	Study group[1] (N = 1 252)			
	non-exposed (N = 209)	low-exposed (N = 408)	medium-exposed (N = 181)	high-exposed (N = 454)
Age [years] (Me)	30	31	32	32
Female/male ratio	142/67	330/78	92/89	136/318
males [%]	32.1	19.1	49.2	70.0
Region and year of the study [n]				
Indonesia				
Kalimantan, 2003 (N = 168)	0	67	31	70
Sulawesi, 2003 (N = 122)	21	17	22	62
Mongolia, 2008 (N = 196)	41	92	13	50
Philippines, 1999 (N = 232)	37	106	50	39
Tanzania, 2003 (N = 218)	31	50	34	103
Zimbabwe, 2004 (N = 193)	36	22	18	117
Zimbabwe, 2006 (N = 123)	43	54	13	13

[1] Non-exposed group – control groups, outside of artisanal and small-scale gold mining (ASGM) areas, with no specific contact to mercury, selected by the national project manager, trying to match to comparable social and economic backgrounds to exposed groups; low-exposed group – living in exposed areas, but not engaged in mining activities related to mercury; medium-exposed group – working with mercury as panners; high-exposed group – working with mercury as amalgam burners.

Health assessment results

Table 6 shows the analysis of the anamnestic data. The participants with higher exposure clearly reported considerably more symptoms compared to the control group. The symptoms included metallic taste, excessive salivation, sleep disturbances, loss of hair, feeling nervous or sad, palpitations, headache, nausea and feeling of numbness. A clear ascending trend between the subgroups could only be shown for some symptoms. The mean values of the special score to assess physical fatigue were 0.49 for the control group, 1.92 for the low-exposed group, 1.79 for the medium-exposed group and 1.69 for the high-exposed group; for the mental fatigue score the mean values were 0.39, 0.84, 0.73 and 0.97, respectively. These scores indicated that the participants from the control group felt physically and mentally better.

Table 6. Clinical data, signs and symptoms of mercury-exposed gold miners

Sign or symptom	Study group[1] [%]				p Chi[2]	p_{trend}
	non-exposed	low-exposed	medium-exposed	high-exposed		
Anamnestic data						
metallic taste	2.4	15.0	19.9	17.8	< 0.000	< 0.000
excessive salivation	6.8	12.5	22.7	23.3	< 0.000	< 0.000
sleep disturbances	12.4	28.7	38.1	25.8	< 0.000	0.009
loss of hair	8.1	34.1	29.3	18.3	< 0.000	0.736
feel nervous	3.1	11.5	11.0	12.9	0.021	0.010
feel sad	6.2	19.1	16.1	19.9	0.004	0.006
palpitations	10.1	14.3	21.2	21.7	0.009	0.001
headache	13.2	37.1	41.0	27.7	< 0.000	0.192
nausea	4.7	18.6	19.5	14.8	0.002	0.123
feel numbness	7.0	26.7	32.2	27.1	< 0.000	< 0.000
Clinical data						
grey to bluish discoloration of oral cavity	6.7	17.2	25.4	23.8	< 0.000	< 0.000
finger to nose tremor	5.3	18.2	15.6	12.4	< 0.000	0.465
heel to shin intentional tremor	4.3	26.3	20.8	9.9	< 0.000	0.147
ataxia of gait (walking)	11.5	30.7	21.0	35.9	< 0.000	< 0.000
heel to shin ataxia	8.5	36.4	37.5	31.5	< 0.000	0.001
dysdiadochokinesia	17.3	37.9	41.1	35.0	< 0.000	0.002
abnormal quadriceps reflex (knee)	12.4	18.6	23.7	22.5	0.030	0.007
abnormal mento-labial reflex	26.9	20.1	16.1	27.4	0.033	0.361
bradykinesia	3.4	9.0	19.0	16.5	0.001	< 0.000
hypomimia	2.4	6.2	12.7	16.2	< 0.000	< 0.000
proteinuria	10.8	12.6	15.6	11.1	0.471	0.932

[1] Study groups as in Table 5.
Chi[2] test p < 0.05 is significant.

The differences between the exposed groups were smaller and without a clear trend.

The analysis of the clinical data (Table 6) showed the prevalence of the typical symptoms of chronic mercury exposure, such as grey to bluish discoloration of the oral cavity, tremor (finger to nose and heel to shin intentional tremor), ataxia (gait and heel to shin ataxia), as well as coordination problems (dysdiadochokinesia). Some reflexes were abnormal, such as the knee jerk and the mento-labial reflex. It was also possible to observe bradykinesia and hypomimia, the symptoms reflecting the fatigue of the exposed participants. Once again there was usually a strong difference between the control group and the exposed groups, whereas the trends from non- to high-exposed groups were not so obvious. Proteinuria did not show any trend.

The neuropsychological data was analyzed (Table 7) using the Kruskal Wallis test, which identified significant differences between all subgroups for the memory test, the matchbox test and the pencil tapping test, but not for the Frostig test. With the help of the Mann-Whitney test it was possible to show that mainly the high-exposed group had statistically poorer results for the memory test,

Table 7. Neuropsychological data of mercury-exposed gold miners

Test	Study group[1]			
	non-exposed	low-exposed	medium-exposed	high-exposed
Memory test				
respondents [n]	125	262	155	389
score				
M±SD	2.0±1.4	2.3±1.2	2.3±1.2	2.5±1.1
Me[###]	2	2*	2 (n.s.)	3***
Matchbox test				
respondents [n]	199	385	176	450
score				
M±SD	19.4±4.6	19.9±4.9	20.7±5.1	21.3±5.1
Me[###]	19	19 (n.s.)	20*	21***
Pencil tapping test				
respondents [n]	198	385	177	447
score				
M±SD	57.4±11.3	56.0±9.8	54.7±10.9	53.1±11.6
Me[###]	59	57 (n.s.)	57*	54***
Frostig test				
respondents [n]	88	156	105	350
score				
M±SD	10.2±1.8	9.8±2.5	10.1±2.4	10.4±2.2
Me (n.s.)	10.5	10.0 (n.s.)	10.0 (n.s.)	11.0 (n.s.)

M – mean; SD – standard deviation; Me – median; n.s. – not statistically significant.
[1] Study groups as in Table 5.
Mann-Whitney test (each exposed group vs. control group): * p < 0.05; *** p < 0.001.
Kruskal Wallis test (difference between any group): ### p < 0.001.

the matchbox test and the pencil tapping test, but not for the Frostig test. This analysis indicated that the exposure to mercury impaired short term memory and coordinative functions. The Frostig test seemed inadequate to detect effects related to mercury exposure.

Mercury analysis in urine, blood and hair

The mercury levels in urine, blood and hair were significantly different in the 4 exposure groups (Table 8). The participants in the different control groups had low mercury levels in all specimens, in general below HBM I levels. The participants in the low-exposed groups had increased mercury levels in all specimens, especially in urine. The participants in the medium- and high-exposed groups had the highest levels. Urine mercury levels in the high-exposed groups were in some cases even extremely high. Blood levels showed the same trend that depended on the exposure group, but were not as high as the urinary levels. Hair showed the same trends, but the levels were not so high. The different specimens do correlate well with each other (Table 9) In a former article we have described these data in detail [16].

Further results

Possible confounders were analyzed: age, gender, dental amalgam fillings, fish consumption and alcohol intake. Age was comparable in the subgroups. Gender analysis showed that the anamnestic symptoms were more prominent with

Table 8. Laboratory data of mercury-exposed gold miners

Examined material	Study group[1]			
	non-exposed	low-exposed	medium-exposed	high-exposed
Urine				
respondents [n]	208	406	181	452
Hg [µg/l]				
M±SD	0.64±1.14	7.95±44.7	25.90±92.7	69.40±288
Me###	0.10	2.30***	6.41***	12.0***
min.–max	< LOD–8.78	< LOD–874	< LOD–868	<LOD–5 240
95% percentile	3.16	22.1	70.8	274
respondents [n]	156	398	179	447
Hg [µg/g creatinine]				
M±SD	0.77±1.45	5.62±19.8	18.80±51.3	36.4±105
Me###	0.20	1.89***	4.36***	9.13***
min.–max	< LOD–9.31	< LOD–355	< LOD–409	< LOD–1 697
95% percentile	3.57	18.9	79.6	143
Blood				
respondents [n]	165	353	168	438
Hg [µg/l]				
M±SD	3.42±4.99	6.47±12.3	12.5±19.3	17.3±37.3
Me###	0.94	3.64***	7.74***	7.56***
min.–max	< LOD–31.3	< LOD–172	< LOD–145	429
95% percentile	14.3	19.8	42.6	56.4

Table 8. Laboratory data of mercury-exposed gold miners – cont.

Examined material	Study group[1]			
	non-exposed	low-exposed	medium-exposed	high-exposed
Hair				
respondents [n]	189	399	177	411
Hg total [μg/g]				
M±SD	1.22±3.33	2.72±7.01	11.0±65.7	8.49±23.3
Me###	0.21	1.23***	2.72***	2.40***
min.–max	< LOD–34.7	< LOD–103	< LOD–792	< LOD–239
95% percentile	4.13	7.32	19.9	33.1
respondents [n]	37	126	91	287
Hg organic [μg/g]				
M±SD	0.78±0.81	2.05±5.29	7.46±39.4	2.83±6.53
Me###	0.27	0.99**	1.26***	1.18***
min.–max	< LOD–3.35	< LOD–51.1	< LOD–326	< LOD–83.3
95% percentile	2.11	5.55	5.86	10.5
respondents [n]	37	126	91	287
Hg inorganic [μg/g]				
M±SD	0.18±0.34	2.69±7.10	9.87±52.5	8.07±23.2
Me###	< LOD	0.64***	0.91***	1.38***
min.–max	< LOD–1.97	< LOD–52.1	< LOD–466	< LOD–225
95% percentile	0.77	13.8	13.4	32.1

min. – minimal value; max – maximal value; LOD – limit of detection.
Other abbreviations as in Table 7.
[1] Study groups as in Table 5.
Laboratory data Mann-Whitney test (exposed groups vs. control group): ** $p < 0.01$; *** $p < 0.001$; Kruskal Wallis test: ### $p < 0.001$.

women, while clinical symptoms were to a lesser extent more common with men.

Twenty-four out of 1252 participants had dental amalgam fillings, 15 of them in the control group, 4 in the low-exposed group, 4 in the medium-exposed group and one in the high-exposed group.

In the Philippines and Indonesia, fish consumption is very common, whereas fish is less commonly consumed in Tanzania and Zimbabwe. In Mongolia, fish is rarely consumed. A correlation test showed that higher fish consumption was statistically significantly associated with higher mercury levels, especially in blood and hair (only organic mercury in hair) (Table 9). This correlation was also significant, but with a relatively low correlation coefficient of 0.319, between fish consumption and medical score sum.

Alcohol ingestion can cause severe neurological symptoms. The separate analysis for female/male participants of the 4 subgroups did not show any significant difference between the men and women [45]. For this analysis, alcohol was not considered as a confounder. The main outcome is the prevalence rate of mercury intoxication in the different exposure groups. We used an algorithm to decide upon intoxication. The analysis showed significantly different prevalence rates for the 4 subgroups (Table 10).

Table 9. Correlation between Hg levels and medical score sum of mercury-exposed gold miners

Variable	Fish consumption	urine μg/l	urine μg/g creatinine	blood [μg/l]	total	hair [μg/g] organic	hair [μg/g] inorganic
Medical score sum							
correlation coefficient	0.319**	0.211**	0.106**	0.220**	0.095**	-0.053	0.074
significance level (2-tailed)	0.000	0.000	0.000	0.000	0.003	0.218	0.086
respondents [n]	1 244	1 247	1 180	1 124	987	541	541
Fish consumption							
correlation coefficient		0.168**	-0.009	0.545**	0.245**	0.181**	-0.070
significance level (2-tailed)		0.000	0.747	0.000	0.000	0.000	0.105
respondents [n]		1 239	1 172	1 116	980	535	535
Hg in urine [μg/l]							
correlation coefficient			0.927**	0.579**	0.671**	0.278**	0.764**
significance level (2-tailed)			0.000	0.000	0.000	0.000	0.000
respondents [n]			1 180	1 120	983	539	539
Hg in urine [μg/g creatinine]							
correlation coefficient				0.487**	0.695**	0.271**	0.791**
significance level (2-tailed)				0.000	0.000	0.000	0.000
respondents [n]				1 064	971	539	539
Hg in blood [μg/l]							
correlation coefficient					0.752**	0.593**	0.696**
significance level (2-tailed)					0.000	0.000	0.000
respondents [n]					865	538	538
Hg in hair [μg/g]							
total							
correlation coefficient						0.687**	0.857**
significance level (2-tailed)						0.000	0.000
respondents [n]						541	541

Table 9. Correlation between Hg levels and medical score sum of mercury-exposed gold miners – cont.

Variable	Fish consumption	urine µg/l	urine µg/g creatinine	blood [µg/l]	hair [µg/g] total	hair [µg/g] organic	hair [µg/g] inorganic
Hg in hair [µg/g] – cont. organic							
correlation coefficient							0.341**
significance level (2-tailed)							0.000
respondents [n]							541

** Spearman's rho.
Correlation is significant at the 0.01 level (2-tailed).

Table 10. Intoxicated respondents in the study of signs and symptoms of mercury-exposed gold miners

Respondents	non-exposed intoxicated [n (%)]	non-exposed not intoxcated [n]	low-exposed intoxicated [n (%)]	low-exposed not intoxicated [n]	medium-exposed intoxicated [n (%)]	medium-exposed not intoxicated [n]	high-exposed intoxicated [n (%)]	high-exposed not intoxicated [n]
				Study group[1]				
Females***	0 (0)	142	59 (17.9)	270	31 (33.7)	61	42 (30.9)	94
Males***	0 (0)	67	25 (32.1)	53	42 (47.2)	47	201 (63.2)	117
Total***	0 (0)	209	84 (20.6)	323	73 (40.3)	108	243 (53.5)	211

Chi² test: *** p < 0.001.
[1] Study groups as in Table 5.

Highest rate was found in the high-exposure group (30.9% of the female participants, 63.2% of the male participants). Second highest rate was found in the medium-exposed group (female 33.7%, male 47.2%). Lower rate was found in the low-exposed group (female 17.9%, male 32.1%). No participant from any control group was found to be intoxcated.

Men were more involved in the mining activities in our project sites. This difference might have been due to different exposure severity; men spend more time mining and are more likely to smelt the amalgams.

DISCUSSION

The results showed clearly that mercury exposure in ASGM areas leads to increased levels of mercury for the participants living in mining areas, and high to very high levels for participants working with mercury either as panners or amalgam burners. The participants developed typical neurological symptoms of chronic mercury intoxication depending on the severity of exposure.

Confounders

Age was not a significant confounder. Dental amalgam fillings were more common in the control groups. In control areas it is more likely to have a functioning health care service, whereas in ASGM areas health care hardly exists. This might explain the higher number of dental amalgam fillings in the control group. Dental amalgam fillings might contribute to the mercury body burden (increase the Hg level). Therefore, dental amalgam fillings cannot explain the higher mercury levels in exposed groups or the higher number of signs and symptoms. Dental amalgam fillings are therefore no confounding factor. Gender had an influence; women reported more frequently subjective symptoms compared to men, whereas objective symptoms were more likely with men. Perhaps women were more aware of their subjective wellbeing whereas men, due to the more severe mercury exposure, developed more symptoms.

Some of the results showed that the low-exposed group in particular exhibited more signs compared to the high-exposed group. One of the possible explanations for this might have been the healthy worker effect. Higher fish consumption was correlated with higher mercury levels, especially in blood and hair. Alcohol consumption did not seem to be a confounder.

The respective project reports included statistical control of confounder and these confounders had no impact on key results presented in this paper. Furthermore a master thesis, explicitly focusing on different statistical methods to reanalyse the data, showed that confounders have no influence on the selection of the key signs and symptoms [45].

Results

As shown in Table 8, the mercury levels in urine, blood and hair were significantly different in the 4 exposure groups. The mercury levels were higher in Zimbabwe 2004, Indonesia and the Philippines, where mining activities were much stronger, compared to Tanzania, and mainly Mongolia and Zimbabwe 2006 with less intensive mining activities. The inorganic mercury vapor from mining was reflected in the very high levels of mercury in urine in the groups of high-exposed participants, the amalgam burners. Hair mercury levels reflect more methyl-mercury, for which the main pathway was fish consumption.

The correlation between the mercury levels in urine, blood and hair was statistically significant (Table 9). Blood results correlated closely with urine and all hair results. This was an indication that mercury in urine reflected more the acute exposure to elemental mercury. The main exposure was likely to be the elemental mercury vapor from burning amalgams, other important pathways were the environmental exposure in mining areas from panning with mercury, storing mercury in an insecure way at home and mercury releases from unprotected tailings. Organic mercury in hair reflected the additional exposure

to methyl-mercury through fish consumption. Inorganic mercury in hair was related to the exposure from working with mercury. Total mercury in hair was an indicator for both, fish consumption and the long-term work exposure. To analyze this further, we took the different signs and symptoms and used the Mann-Whitney test to find out if the signs and symptoms were associated with the mercury levels (results not shown).

The symptom of metallic taste was statistically significantly associated with all specimen results, whereas symptoms such as excessive salivation, sleep disturbances and loss of hair were only associated with mercury levels in hair. The signs of ataxia of gait and heel to shin tremor were statistically significantly associated with all specimen results. The signs of grey to bluish discoloration of the oral cavity, finger to nose tremor, heel to shin ataxia, quadriceps reflex, mento-labial reflex were more likely to be related to mercury in hair or blood. Interestingly, many of these signs and symptoms were more closely associated with organic than inorganic mercury. May be this was an indication that inorganic mercury was transformed over the time into organic mercury. This hypothesis was supported by the fact that nearly all signs and symptoms were respectively associated with the total years of mercury exposure. This association between years of exposure and the different signs and symptoms was stronger compared to mercury levels in urine, blood and hair.

Neurological signs and symptoms developed slowly and depended on the dose as well as on the duration of exposure to mercury. Miners were not in a steady state of exposure. Therefore it was very likely that the association between long term and intensive exposure and chronic neurological signs and symptoms is causal. The medical score was statistically significantly associated with the total years of exposure (Mann-Whitney test p < 0.001) (boxplot – Figure 1). The health problems differed between the different mining areas. The percentage of intoxicated male miners was 89.5% for Zimbabwe 2004, 78.8% for the
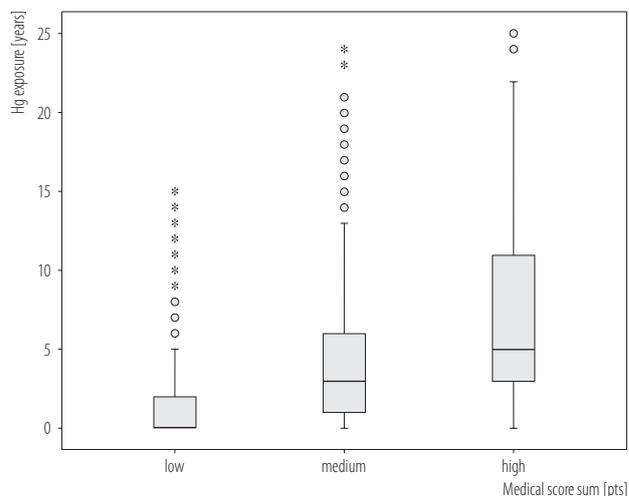
* Low = 0–4, medium = 5–9, high = 10–21.

Fig. 1. Medical score sum* and total years of mercury exposure of gold miners

Philippines, 68.6% for Indonesia–Kalimantan, and 23.5% for Tanzania. This reflected the diverse extents of exposure of miners and community members due to different capacities to extract and mill ore, as well as the varying amounts of mercury used to process the ore.

In general, more men were intoxicated compared to women. The reason for this was that men were more likely to practice amalgam burning, whereas women were more likely to break the ores and perform the panning process.

This unhealthy and dangerous mercury exposure in the immediate environment needs to be urgently reduced. There are technical alternatives to reduce the exposure [50]. Methods are also being developed to replace mercury in ASGM, e.g., with the so-called gravity-borax method [51,52].

The capabilities of health care systems in the sometimes remote areas are not sufficient to diagnose or treat chronic mercury intoxication. Laboratory capacities are only rarely available that can analyze mercury in urine alone. Health care providers have insufficient knowledge of the signs and symptoms of chronic mercury intoxication. Health care systems need to be prepared for this emerging

problem of chronic mercury intoxication among exposed population in ASGM areas.

Literature

There are a number of publications available that address the issue of Hg as a health hazard in ASGM. Recently, a good review article was published [23]. This detailed article summarized the results from 26 studies, showing that the exposure to inorganic Hg vapor is high, and that toxic effects have to be considered. Some relevant papers in different countries with ASGM showed that Hg levels in any analyzed biomarker were higher compared to control groups or reference values, and in some studies clinical symptoms or negative results for subclinical parameters were identified [7,8,13,14,26,28,29,31,32,53–60]. These results are very similar to our results.

Limitations

This study was based on several different health assessments. All these studies used the same key questions in the questionnaire, same medical and neuro-psychological tests [61]. Not all health assessments had used all parameters. For example parameters that did not show any relevance were deleted in later-on studies, and additional new parameters tested. The risk groups differed, in general men, women and children were assessed (Philippines, Indonesia, Tanzania, Zimbabwe 2004); in Zimbabwe 2006 the risk group was mother-child pairs, and in Mongolia women at child bearing age (Table 1).

There might be biases, since the questionnaire surveys were performed by different nurses, the neuropsychological tests were done by different experts, but the examiner of the medical tests was always the same. Other bias might be due to imperfect information recall by exposed participants or controls. Miners did not work continuously with mercury; some workers might have been exposed nonstop, other just periodically. The main result of the reports from all surveyed countries was similar: high-exposed miners showed typical neurological signs and symptoms of chronic mercury intoxication.

Non-exposed participants were not selected at random; the selection was based on the experience of the national project manager to identify non-mercury-exposed participants with similar social and economic background. Nevertheless, with 1252 participants, this is by far the largest cross-sectional cohort in ASGM areas. And this fairly big size of participant group facilitated the statistical analyses of data.

CONCLUSIONS

Chronic mercury intoxication, with tremor, ataxia and other neurological symptoms together with a raised body burden of mercury was clinically diagnosed in artisanal small-scale mining areas. Primary prevention is necessary, mercury exposure needs to be urgently reduced using available technical alternatives [50]. Health care systems need to be prepared for this emerging problem of chronic mercury intoxication among exposed people. It will be useful to develop a simplified screening tool to identify mercury-related health symptoms as early as possible.

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