

Institute of Forensic Medicine Ludwig-Maximilians-University Munich, Germany

Mercury as a health hazard due to gold mining and mineral processing activities in Mindanao/Philippines

- Final report -

Munich 15th of April 2000

STEPHAN BÖSE-O'REILLY, STEFAN MAYDL, GUSTAV DRASCH, GABRIELE ROIDER

UNIDO Project No. DP/PHI/98/005

Contract 99/939/TS - Toxicologist for Assessment of mercury levels in humans, mining areas along Naboc and Hijo river, Philippines

Contract 99/055/IR- Assistance in reducing mercury emissions in highly contaminated areas in Mindanao

Contents

STUDY SETTING AND CLINICAL EXAMINATIONS (S. BÖSE-O'REILLY)	4
Introduction	4
Gold rush in the area of Mount Diwata	4
Study design	6
Questionnaire	6
Neurological examination	7
Neuro-psychological testing:	8
Specimens	8
Malaria smear	8
• Urine protein test	8
Clinical impression	9
Clinical symptoms	9
Clinical subgroups	10
SPECIMEN ANALYSIS AND STATISTICAL RESULTS (GUSTAV DRASCH)	12
Laboratory methods	12
Material and Method	12
Sample Preparation	12
Statistical methods	13
Statistical analysis	14
Description of mercury levels in urine, blood and hair	14
Exclusion of data	16
Subgroups due to residence and occupation	16
Reducing of redundant data for statistical analysis	17
Alcohol as a possible bias factor	18
Scoring of medical results	20

Statistical analysis of mercury levels in urine, blood and hair	22
Statistical analysis of mercury levels versus clinical data	22
Discussion of the statistical analysis	23
Mercury levels compared to toxicological threshold limits	24
German Human-Biomonitoring (HBM) Values for Mercury	24
Occupational threshold limits (BAT, BEI)	26
Decision for the diagnosis of a "chronic mercury intoxication"	27
Prevalence of the diagnosis Mercury intoxication	29
Influence of working conditions	30
Influence on Pregnancy	32
CONCLUSIONS (GUSTAV DRASCH. STEPHAN BÖSE-O'REILLY)	34
Health problems around Mt Diwata, not related to mercury	34
Mercury as a severe health hazard	34
Further investigations, which still will be performed with the specimen achieved for this study	35
Mercury intoxication treatment	36
Suggestions	37
Medical treatment	37
Further Suggestions	39
Literature:	41
Appendix 1: Figures	45

Appendix 3: Coding Instruction

Study setting and clinical examinations (Stephan Böse-O'Reilly)

Introduction

The heavy metal mercury is a health hazard (mercury = Hg). It is widely used in processing gold ore in third world countries like Brazil or the Philippines. Our project run by the United Nations Industrial Development Organization – UNIDO, the Institute of Forensic Medicine of the Ludwig-Maximilians-University of Munich, and the Mines and Geosciences Bureau in Davao, Philippines, investigated the risk of using mercury in a gold rush area on the Philippines. The project was to evaluate the influence of the mercury burden on the local population and the extent of the possible health effects.

Gold rush in the area of Mount Diwata

The Philippines are in South East Asia. On Mindanao, one of the major islands of the Philippines, ore containing gold is mined mainly in the area of Diwalwal. Dominated by the mountains of Mount Diwata, Diwalwal is the heart of a major gold rush area, where approx. 15.000 people live. Gold mining has existed here since more than one and a half decades.

Housing is poor, mainly wooden huts. Tunnels, small industrial complexes (ball-mills, cyanidation plants), shops and housing areas are haphazardly mixed together without any sign of planning. 50% of the huts have no toilets. A proper disposal system of waste including excrement's is missing. Waste is disposed into the river or just dumped. Tuberculosis is the main reason of severe disease and mortality.

At the moment approx. 15.000 people are living in Diwalwal. The **local health centre** of Diwalwal is extremely poorly equipped. Since some years no doctor could be found to work in the health centre. It is run by midwifes and "helots". The health centre is not equipped to diagnose tuberculosis, nor to treat any serious accident. It is absolutely not equipped to diagnose mercury intoxication, nor can it treat such a condition.

To date there are approximately 150 tunnels - some up to 2 km long - in Mount Diwata. They have no proper fresh air ventilation and many accidents occur. Dozens of workers loose their lives each year due to unsafe working conditions. Rival rebel groups for example "New People's Army" and "Moro National Liberation Front", mine in the same area which leads to major outbreaks of violence. This violence is the second major cause of morbidity and mortality. Within approx. 100 workers taking part in the study, 4 of them had severe gun shot injuries. One child was shot accidentally at the age of one year and lost one arm.

The ore from the mines is ground to powder in small companies while still in Diwalwal. As already mentioned, these ball-mills are within the housing areas in this town. Liquid mercury is added to the powder to extract the gold in order to achieve an amalgam connection of gold and mercury.

To extract the gold the amalgam is heated in local small companies or in private homes. The vaporised mercury is another source of mercury burden on the regional population. Tailings containing mercury can be found in the whole region. These tailings are transported by wind or water into the ecosystem:

Chicken and pigs roam freely within the contaminated areas of the ball-mills.

The grey Naboc waters flow down from Diwalwal. Downstream from Diwalwal is Monkayo, situated in a very fertile plain. Rice, bananas, vegetables, fruit and cattle are important local products. Naboc river water is also used to irrigate the rice fields and other crops. Cattle drink this water too. The local population eat up to three times a day fish, which is highly contaminated with mercury.

5

Study design

To evaluate the influence of this mercury burden on the local population and the extent of the possible health effects, we examined 323 participants. These participants consisted of: workers from Diwalwal, local families from Monkayo (Naboc, Tubo-Tubo, Babag and Mamunga) including children and a control group in Davao. The workers were mainly mercury exposed ball-millers and amalgam smelters. Miners were intentionally excluded. It could be expected that their mercury burden was a similar order of magnitude than of other (non occupationally mercury exposed) inhabitants of Mount Diwata. But many of the health problems of the miners may derive from their hard underground work. Therefore it would be almost impossible to distinguish in this group between negative health effects caused by mercury and by mining.

The examinations took place in a room in the local "Women's Centre " in Monkayo . Team members from MGB (Johnny Calvez, Lolit Broces, Alfredo Relampagos), the Monkayo Health Centre (Dra. Kapora, Baluis Rizal, Babiano Ricardo, Ababa Anelisha, Corotan Angelita, Febrey Dave Pinggoy, Aley Renomerow) and Mr. cand. med. Stefan Maydl (Germany) performed the examinations under the direction of Dr. med. Stephan Böse-O'Reilly. The participants from Diwalwal and Monkayo all received a per diem (UNIDO/MGB) and a nice gift in the form of a T-shirt (donation of Smith-Kline-Beecham Germany).

A written consent of every participant was achieved before performing any examination.

Questionnaire:

The participants filled in a questionnaire with assistance from midwifes or nurses. Questions included:

- Working in a gold plant or mineral processing plant?
- Working with mercury or with mercury polluted tailings?

- Burning amalgam in the open?
- Melting gold in the open or with inadequate fume hoods?
- Drinking alcohol?
- Having a kind of a metallic taste?
- Suffering from excessive salivation?
- Problems with tremor / shaking at work?
- Sleeping problems?

Neurological examination

All participants were clinically, mainly neurologically examined. Results were mainly primarily scored according to "Skalen und Scores in der Neurologie" (Masur 1995):

- Signs of bluish discoloration of gums
- Rigidity and ataxia (walking or standing)
- Tremor: tongue, eye-lids, finger to nose, pouring, posture holding and the Romberg test
- Test of alternating movements or test for dysdiadochokinesis
- Test for irregular eye movements or so called nystagmus
- Test of the field of vision
- Reflexes: knee jerk reflex and biceps reflex
- Pathological reflexes: Babinski reflex and sucking reflex
- Salivation and dysathria
- Sensory examination

Neuro-psychological testing:

- The following tests were carried out (Zimmer 1984, Lockowandt 1995, Masur 1996)
- Memory disturbances: Digit span test (Part of Wechsler Memory Scale) to test the short term memory
- Match Box Test (from MOT) to test co-ordination, intentional tremor and concentration
- Frostig Score (subtest la 1-9) to test tremor and visual-motoric capacities
- Pencil Tapping Test (from MOT) to test intentional tremor and co-ordination

Specimens

The following specimens were taken, and two tests (malaria and proteinuria) were performed immediately:

- Blood (EDTA-blood 10 ml)
 Malaria smear: None of the participants had a positive malaria smear.
- Urine (spontaneous urine sample 10 ml)
 Urine protein test: Results see below
- Hair

The specimens urine and blood were cooled after collection until arrival in the laboratory in Munich, Germany. Video and photo documentation of the examinations was carried out.

Clinical impression

Clinical symptoms

Some of the participants showed very severe symptoms.

- Moderate walking disturbances with ataxia was mainly seen, when the test was performed with closed eyes.
- Moderate tremor while standing still with arms outstrechted, wrist mildly extended, fingers spread apart – the Romberg test.
- Moderate tremor with the finger to nose test was mainly seen, when the test was performed with closed eyes. Co-ordination problems could also be observed with this test.
- When the participants twisted their hands very quickly and had at the same time their eyes closed, the problem of alternating movements or dysdiadochokinesis was very obvious.
- Also an impressive tremor of the tongue could be observed.
- A severe tremor of the eye lids was a visible, severe symptom of a mercury intoxication.
- Another pathological symptom to be observed was a strong positive knee jerk reflex, with a very wide reflex zone.
- A common pathological reflex in our study group was a positive sucking reflex.
- The blue-toned discoloration of the gums was an impressive and typical symptom of mercury intoxication.
- Finally we observed some participants with a hypomimic. The participant had a very passive attitude. The facial expression showed no signs of emotion. They just sat and waited.

Clinical subgroups

Our clinical impression was, that a fair amount of **workers** from Diwalwal showed severe symptoms that could very well be related to the classical picture of a mercury intoxication. They reported about fatigue, tremor, memory problems, restlessness, loss of weight, metallic taste and sleeping disturbances. We found intentional tremor, mainly fine tremor of eye lids, lips and fingers, ataxia, hyperreflexia and sensory disturbances as well as a bluish discoloration of the gums. It should be noted that the workers from Diwalwal certainly were primarily very healthy and strong young men (healthy worker effect). We may not have seen the most severe cases, since the people from Diwalwal had to come down to Monkayo for examination (2 hours journey). Due to a lack of a highly developed social system in the Philippines, some very sick workers might have moved back to their original homes and families in other areas on the Philippines.

The participants from the low land area of **Monkayo** and surrounding barangays showed less clinical signs. They complained more about other symptoms, which could be related to mercury, such as: headache, vision problems and nausea.

The control group in Davao - staff from the local Mines and Geoscience Office - were healthy and did not show signs of any special health problems.

One third to one quarter of the population in Diwalwal are children. The main health problem of **children** in Diwalwal seem to be:

High exposure to mercury in the area. Children to have access to fluid mercury, they play with their hands with this mercury. They live within the houses where ball-milling or amalgam smelting is carried out, therefore they are also exposed to the mercury fumes.

Beginning at the age of seven or eight, children start to work in the area, carrying sacks with rocks, ball-milling, hammering rocks to smaller pieces and many other

activities. It seems, the children do not work any longer within the tunnels, (as they used to do in earlier years). But it is still **child work** in the very early years of life. It is physically very hard work, and the children are related to a high exposure level of mercury. Accidents related to work are a health hazard for these children.

High risk of tuberculosis exposure is also a mayor health hazard. Due to poor sanitary conditions, infectious diseases like gastro-intestinal infections and pneumonia are still very common and are a mayor reason of infant mortality.

Specimen analysis and statistical results (Gustav Drasch)

Laboratory methods

Material and Method

Material and Sample Storage

From 323 participants on the Philippines 323 blood samples, 313 urine samples and 316 hair samples were taken by Dr. Böse-O'Reilly. The blood samples were taken in EDTA-coated vials. The urine samples were acidified with acetic acid. To avoid degradation, all samples were stored permanently and transported by flight to Germany in an electric cooling box. Until analysis the samples were stored continuously at 4 °C.

Sample Preparation

<u>Hair:</u> In all cases the scalp near part from 0 - 3 cm of the hair was selected. 150 – 250 mg of these hair segments were treated with 1.0 ml nitric acid (min 65%, suprapur grade, E. Merck, Darmstadt, Germany) in polypropylene test tubes, locked with screw caps for approximately 12 hours at 50 °C in a heating block. After cooling, the clear solutions were filled up to 5.0 ml with redistilled water and vortexed. Aliquots of these solutions were analyzed. Intentionally washing steps with water, detergents or organic solvents like acetone were not performed before the solution. Washing procedures with different solvents are frequently applied before hair analyses with the aim to remove air-borne heavy metal pollution from the surface of the

hair. But as shown in literature, a distinct differentiation between air-borne and interior mercury cannot be achieved which such washing procedures (Kijewski 1993). Orientating pre-experiments with washing the hair samples from the Philippines supported this assumption. After washing some samples from the same strain totally unreproducible results were obtained. Therefore the hair samples were dissolved without any further pretreatment.

<u>Blood, urine:</u> Aliquots of up to 1.0 ml were measured directly without further pretreatment. This was possible, because sodium-borohydride was applied for the mercury reduction and all nascent mercury vapour was inter-collected on a gold-platinum-net (method see below).

Mercury determination and quality control

The (total) amount of mercury in the samples was determined by means of so-called cold-vapour atomic absorption spectrometry (CV-AAS), using a Perkin-Elmer 1100 B spectrometer with a MHS 20 and an amalgamation unit. The determination limit for Hg in blood or urine was 0.25 μ g/l, for Hg in hair 0.01 μ g/g.

All analyses were performed under strict internal and external quality control. The following standard reference materials served as matrix-matched control samples: human hair powder GBW No. 7601 (certified Hg 0.36 \pm 0.05 µg/g) and Seronorm whole blood No. 203056 (certified Hg 8.5 – 11.5 µg/l).

Statistical methods

Statistics were calculated with the SPSS 9.0 programme (SPSS-software, Munich, Germany). As expected, the mercury concentrations in the biomonitors (blood, urine, hair) were not distributed normally but left-shifted. Therefore in addition to the arithmetic mean (only for comparison to other studies) the median (50% percentile) is given. For all statistical calculations distribution-free methods like the Mann-Whitney-

U-test for comparing two independent groups or the Spearman rank test for correlation were used. "Statistically significant" means an error probability p < 0.05 (5%).

Some graphs were shows as so-called "box-plots". For a brief explanation: The "box" represents the interquartile (this means from the 25% to the 75% percentile). The strong line in the box is the median (50% percentile). The "whiskers" show the span. Out-rulers are indicated by dots.

Statistical analysis

Description of mercury levels in urine, blood and hair

In table 1 the (total) mercury concentration of all analysed blood, urine and hair samples is summarised. For comparison the results for blood and urine from a representative epidemiological study, performed 1990/92 in Germany (Krause 1996) are reported in the same table. For a better comparison of the hair values, recently published own data from Germany are cited (Drasch 1998). In recent literature from Europe and Northern America similar Hg concentrations in blood, urine and hair have been reported. From populations with a high consumption of methylmercury-contaminated sea food like in Japan, the Faroes Islands, the Seychelles or Canadian Inuits higher Hg values in the biomonitors have been reported recently e.g. on the International Conferences on "Mercury as a Global Pollutant" 1996 in Hamburg, Germany and 1999 in Rio de Janeiro, Brazil (for literature in detail see proceedings). From other areas with small scale gold mining like in the Amazon, Brazil, but also on the Philippines (Akagi 1999) mercury concentrations, comparable to ours, have been reported e.g. at these congresses or summarised in the book "Mercury from Gold and Silver Mining: A Chemical Time Bomb?" by de Lacerda and Salomons (1998).

		Philippines	Germany
		(this study)	(for comparison)
Hg-blood (µg/l)	case number	323	3958
	span	< 0.25 - 107.6	< 0.2 - 12.2
	median	8.2	0.6
	arithm. mean	11.48	0.51
Hg-urine (µg/l)	case number	313	4002
	span	< 0.25 – 294	< 0.2 - 53.9
	median	2.5	0.5
	arithm. mean	11.08	1.11
Hg-urine (µg/g crea)	case number	313	4002
	span	< 0.1 – 196.3	< 0.1 – 73.5
	median	2.4	0.4
	arithm. mean	8.40	0.71
Hg-hair (µg/g)	case number	316	150
	span	0.03 – 37.76	0.04 – 2.53
	arithm. mean	4.14	
	median	2.72	0.25

Table 1: Concentration of total mercury in blood and urine (Krause 1996), and hair (Drasch 1997)

All mercury concentrations in the different biomonitors blood, urine and hair are highly significant rank correlated (table 2). Despite this, the individual values scatter widely (see figures 1,17-20).

Hg-urine (µg/l)	r _o = + 0.58 n = 313 ***		
	$r_{o} = + 0.56$	$r_{o} = + 0.88$	
Hg-Urine (µg/g crea)	n = 313	n = 313	
	***	***	
	$r_{o} = + 0.61$	$r_{o} = + 0.34$	$r_{o} = + 0.39$
Hg-hair (µg/g)	n = 316	n = 311	n = 311
	***	***	***
	Hg-blood (µg/l)	Hg-urine (µg/l)	Hg-urine (µg/g crea)

Table 2: Spearman rank correlation between (the mercury concentration in the different biomonitors (r_o = rank correlation factor; n = case nimber; *** = p < 0.001)

Exclusion of data

From the total group 16 cases had to be excluded from further statistical analysis:

- 9 cases from the control group, due to missing data (only blood samples could be taken in these cases without any further medical or neurological investigation)
- 7 due to possible bias: these participants showed severe neurological diseases, like stroke or Parkinson's disease, and would bias the results.

Forming subgroups due to residence and occupation

To distinguish between the possible sources of mercury burden, we formed subgroups. The remaining group of 307 participants was subdivided due to residence and occupation criteria. The following subgroups were formed:

1. **Control**: 42 participants from Davao, without special Hg burden.

- 2. **Downstream**: 100 participants living in the barangays of Mamunga, Babag, Tubo-Tubo and Naboc in the Monkayo area at the base of Mt. Diwata. They may be secondary Hg-burdened, especially by Hg-contaminated water flowing down from Mt. Diwata. Excluded from this group are a few persons from this area, which may be occupationally Hg burdened. Those are grouped in 4 and 7.
- 3. **Diwata, no Hg occupation**: 43 participants, living in Diwalwal without any special occupational Hg-burden.
- 4. **Diwata, possibly Hg exposed by family**: 20 family members possibly exposed by Hg, brought home with Hg contaminated clothes etc.
- 5. Diwata, ball-millworkers: 55 workers in ball mills
- 6. Diwata, amalgam smelter: 41 workers, smelting gold-amalgam
- 7. **Diwata, other Hg occupation**: 6 participants, which have declared that they have occupationally contact to Hg, but do not belong to group 5 or 6.

Unless other indicated, all further statistical analysis was performed with these subgroups.

Reducing of redundant data for statistical analysis

From the extremely large data volume, collected in field by Dr. Böse-O'Reilly, the relevant facts and test results were selected by pre-investigations (see appendix). Many test results were primarily scored (for instance: no, moderate, strong, extreme). For the anamnestic and clinical data these results could be reduced to a yes/no decision, which enables a statistical analysis and facilitates the readability of table 3 (in appendix) markedly without a relevant loss of information. The neuro-psychological data (memory, match-box, Frostig, finger tapping) was reduced according to a box-plot procedure. With this procedure the results of the participants could be divided into three categories: The best performing 25% of participants of each group

were given a score of 0 points, the worst performing 25% of participants were given a score of 2 points and the middle group of participants received a score of 1 point. In table 3 the results of the statistical analysis of the transformed anamnestic, clinical and neurological data versus the different Hg-burdened subgroups, is shown. The significance of the differences was calculated with Chi-square test (* p<0,05, ** p<0,01, *** p<0,001).

In the figures 2-5 some subjective (health problems worsened since Hg exposure) and objective (ataxia, tremor, bluish coloration of the gingiva) criteria, typical for a chronic mercury burden are figured graphically. It is striking that in comparison to the control group from Davao, many test results even from the non occupationally Hg-burdened population, living on and downstream from Mt. Diwata are considerably worse. The negative results increase even more in the occupational Hg-burdened groups of ball millers and amalgam smelters. In some tests the negative results of the participants with Hg-burdened family members exceed non-Hg-burdened inhabitants of Mt. Diwata. The results from the mixed occupational group (other Hg occupation) should not be over-interpreted, due to the low case number (only 6) and the inhomogeneity of this group.

Alcohol as a possible bias factor

Due to a bias of other factors than mercury, objections might be raised against our study results. Mainly alcohol could have influenced or biased our results. Every participant was questioned about their alcohol consumption habits. To test for the possible bias, first of all the alcohol consumption rate in the different Hg-burdened subgroups were compared with Chi-square test (in the same manner as the other factors). In result the alcohol consume of the Hg-workers (ball-mill workers, amalgam smelters and other workers) is indeed higher than in the other groups (table 3). But the percentage of adult males in these groups (> 75%) is more significant than in the other populations, too (see table 3). To solve the problem of a bias of alcohol consumption, the total population was divided in two groups:

1. 151 males (> 14 years) 2. 156 children (< 14 years) and females.

In the group of children and women only one female had declared a heavier alcohol consumption. This one female was excluded from the group, resulting in 155 children and women without relevant alcohol consumption. The statistical analysis, as performed with the total group (n = 307) was repeated with this group of children and women (n = 155). As to be expected, the number of Hg workers was low in this group (only 9 ball-mill workers, 4 amalgam smelters). Therefore the residence and occupation subgroups were reduced to control (n = 20), downstream (n = 66), and one Hg-burdened group (Diwata, no Hg occupation & Hg by family & ball-mill worker & amalgam smelter; total n = 69). In result both the downstream and the Hg-burdened group differ significantly from the control group in the same parameters as do the total group of males and females (n = 307). For further control, analogous calculations were performed with the male group (n = 151), too. In principle, comparable results were obtained.

This means, that the higher alcohol consumption of the predominant male Hg-workers in the area of Mt. Diwata does not considerably bias the statistical result as shown in table 3.

Scoring of medical results

The evaluation so far showed statistically significant medical test results versus the different Hg-burdened subgroups. These significant medical test results are typical clinical signs of chronic mercury intoxication, such as tremor, metallic taste, excessive salivation, sleeping problems, memory disturbances and proteinuria (Drasch 1994, Kommission Human-Biomonitoring 1999, Wilhelm 2000). Furthermore ataxia, dysdiadochokinesis, pathological reflexes, coordination problems and concentration problems are clinical signs of a damaged central and peripheral nervous system.

For a further evaluation of these medical results a medical score was established. The factors, included into this medical score and the score-points per factor are shown in table 4. The higher the score total, the worse the health problems of a participant were.

Statistic testing of the different Hg-burdened subgroups versus the total medical score sum showed once again significant results. The results are shown in table 3 and in figure 6 graphically as a box-plot. The scores of all other groups are statistically significantly higher than the control group from Davao (Mann-Whitney-U-Test). Unexpected are especially the high scores (i.e. bad health conditions) of the population living in the villages downstream of Mt. Diwata.

Test	Score Points
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	
bluish coloration of gingiva	0/1
ataxia of gait	0/1
finger to nose tremor	0/1
dysdiadochokinesis	0/1
heel to knee ataxia	0/1
heel to knee tremor	0/1
sucking	0/1
proteinuria	0/1
Neuropsychological tests	
memory test	0/1/2
matchbox test	0/1/2
Frostig test	0/1/2
tapping test	0/1/2
Maximum	21

Table 4: Anamnestic, clinical, neurological and neuro-psychological scoring scale

Statistical analysis of mercury levels in urine, blood and hair

Statistical testing of the different Hg-burdened subgroups versus mercury concentration in blood, urine and hair show significant results (table 3). The differences in the mercury concentration in urine (figure 8) were much more striking than those in blood or hair (figure 7,9). These results were comparable to studies in Bazil, like from Cleary et al. along the Tapjós River (Cleary 1994).

As expected, the highest burden is found in the Hg-occupational burdened groups of ball-mill workers and amalgam smelters, followed by other inhabitants of the Mt. Diwata area. The mercury concentration in blood, urine or hair of family members from mercury workers (group Hg-by-family) are not higher than of other inhabitants of the Mt. Diwata area (group Diwata, no-Hg-occup). But both groups show significantly higher mercury concentrations in urine than the control group from Davao. Surprisingly, the mean blood and hair mercury concentrations in these two groups were lower than in the control group from Davao.

The mercury concentrations in blood and urine of people living downstream in the Monkayo area at the base of Mt. Diwata (group downstream) were lower than in the control region of Davao, whilst mercury in hair was equal.

The mercury concentration in the blood and hair samples from the control group from Davao (n = 42) was unexpectedly high - not only in comparison to the population of Mt. Diwata and the Monkayo area downstream, but also in an international comparison. In contrast to this, the mercury concentration in urine in Davao was in an acceptable range. This distribution (high Hg in blood and hair, moderate in urine) is characteristic for a methyl-mercury burden, e.g. from high mercury burdened marine food.

Statistical analysis of mercury levels versus clinical data

Only some of the medical data correlate significantly to the Hg concentration in blood or urine, none to Hg in hair (Chi-square-test, Mann-Whitney-U-test, Spearman rank correlation): Only the memory test correlates significantly high to Hg in blood as in urine (see figures 10,11). The metallic taste, the complaint about the fact that the health situation has worsened since the beginning of the mercury exposition, the sucking reflex and the frequency of proteinuria (figure 12) correlate at least to Hg-urine, the Frostig test to Hg-blood.

The medical score sum (calculated as shown in table 3) correlated statistically significant to Hg in urine, but not to Hg in blood nor hair. Nevertheless, the figures 13 and 13 show the striking dependence of the medical score sum from the mercury concentration in blood and urine: Almost all cases with higher mercury concentrations in blood and/or urine showed higher medical score sum, i.e. worse health condition.

Discussion of the statistical analysis

The relatively poor correlation of classic clinical signs for a mercury intoxication to the mercury concentrations in the bio-monitors (blood, urine, hair) may be explained by several factors:

- The mercury concentration in the target tissues, especially the brain, correlate to the mercury concentration in bio-monitors like urine, blood or hair. This correlation is statistically significant and good enough to mirror different burden of different groups (here e.g. workers and non-workers). But the <u>inter-individual</u> <u>differences</u> are so large that it is rather pointless to conclude the heavy metal burden in the target tissue of an individual from the concentration in the biomonitors (Drasch 1997).
- From the situation a mixed burden with <u>several mercury species</u> must be assumed: For instance on Mt. Diwata a combination of mercury vapour (in the air), inorganic mercury (in the soil) and probably in addition methyl-mercury from local fish, caught in the Monkayo region. The toxicological effects and potentials of these different mercury species differ widely.

 In most cases the people are <u>chronically burdened</u> by mercury and not only acute. This means that a reversible or even irreversible damage of the central nervous system may be set months or years before the actual determination of the mercury concentration in the bio-monitors under a quite different burden.

Mercury levels compared to toxicological threshold limits

In the intentional literature only a few threshold limits for mercury in bio-monitors are recommended, especially for an at least predominant burden with mercury vapour and inorganic mercury, as could be expected in the investigated population. Most studies in this field are performed in populations with a exclusively methyl-mercury burden from fish or sea-food, like the former data from Minamata, or the more recent data from the Seychelles (Davidson 1998), the Faroes Islands (Grandjean 1997) or even from the Amazon (Grandjean 1999). To estimate the toxicological relevance of the mixed burden with metallic, inorganic and organic mercury of the investigated population from Mindanao, the following threshold limits were used:

German Human-Biomonitoring (HBM) Values for Mercury

In 1999 the German Umweltbundesamt published recommendations for referenceand human-biomonitoring-values (HBM) for mercury (Kommission Human-Biomonitoring 1999).

The "**reference values**" only describe the actual Hg-burden in Germany and do not have any toxicological relevance. In contrast to them, the HBM-values are assessed by toxicological considerations:

The HBM I was set to be a "**check value**", this means an elevated mercury concentration in blood or urine, above which the source of the Hg-burden should be searched and, as far as possible, eliminated. But even by an exceeding of this HBM I the authors claimed that a health risk is not to be expected.

In contrast to this, the (higher) HBM II value is an "**intervention value**". This means, at blood or urine levels above HBM II, especially for a longer time, adverse health effects can not be excluded. Therefore interventions are necessary. On the one hand

the source should be found and reduced urgently. On the other hand a medical check for possible symptoms should be performed. For hair, comparable values are not established, but the HBM II in blood is directly derived from the assumption of a stable ratio of mercury in blood and hair (1:300) and the result of the Seychelles study, where adverse effects could be seen at mercury concentration in hair above 5 μ g/g (Davidson 1998). Therefore this value was taken in our study as an analogous value for HBM II for the toxicological evaluation of mercury concentration determined in hair. Again it must be kept in mind, that this threshold limit in hair was established in a population burdened with methyl-mercury from marine food and not with mercury vapour or inorganic mercury species, as is predominant on Mt. Diwata.

In 1991 the WHO expert group stated that mercury in urine is the best indicator for a burden with inorganic mercury. The maximum acceptable concentration of mercury in urine was set to 50 µg/l (WHO 1991). A distinct threshold for mercury in blood was not given. Mercury in hair is widely accepted as best indicator for the assessment of contamination in populations exposed to methyl-mercury (de Lacerda 1998). For this, a maximum allowable concentration of 7.0 µg/g hair was set by the FAO/WHO (EPA 1997). All these limits and others, former published, are respected at the most recent recommendation from the German Umweltbundesamt 1999, as cited above. The high numbers of recently published investigations on mercury burdened populations from gold mining areas like in South-America or by sea food like on the Faroes Islands or the Seychelles require a continuos re-evaluation of toxicologically defined threshold limits. Therefore the international latest recommendation from the German Umweltbundesamt were taken for further comparison. As shown in the next chapter (Decision for the diagnosis of a "chronic mercury intoxication"), for our population with a mixed burden (metallic - inorganic - organic mercury, acute - chronic) the biological threshold limits should not be overestimated for the diagnosis. Therefore the question, which of the limits are best for evaluating the results of this study is only of secondary interest.

	Hg-blood (µg/l)	Hg-urine (µg/l)	Hg-urine (µg/g crea)	Hg-hair (µg/g)
HBM I	5	7	5	
HBM II	15	25	20	5 (in analogy)
WHO		50		7
BAT for metallic and inorganic Hg	25	100		
BAT for organic Hg	100			
BEI (Biological exposure index)	15 (after working)		35 (before working)	

Table 5: Toxicologically established threshold limits for mercury in blood, urine and hair (HBM = Human Bio-Monitoring; BAT = Biologischer Arbeitsstoff-Toleranzwert; BEI = Biological Exposure Indices)

Occupational threshold limits (BAT, BEI)

Other toxicologically founded limits are occupationally threshold limits. Such limits are established for mercury e.g. in the USA (biological exposure indices BEIs of the American Conference of Governmental Industrial Hygienists) or Germany (BAT value, Deutsche Forschungsgemeinschaft 1999). For a better comparison with the HBM-values (which are, to our knowledge, only established in Germany) the German BAT-values for metallic and inorganic mercury are taken for this study. From the definition, these BAT-values are exclusively valid for healthy adult workers under occupational medical control. The occupational burden must be stopped, if this threshold is exceeded. These occupational threshold limits are not valid for the total population, especially not for risk groups like children, pregnant women, older or ill persons. Nevertheless, the BAT-values were taken for a further classifying of our high results, too. BAT-values for mercury are established only for blood and urine, but not for hair. Table 5 gives an overview of the HBM-, BAT- and BEI-values. In Table 3 the percentage of the exceeding of the HBM- and BAT-limits in the various population groups of our study is summarised.

Decision for the diagnosis of a "chronic mercury intoxication"

For the different Hg burdened groups (< HBM I; HBM I - HBM II; HBM II - BAT; > BAT) <u>no</u> striking differences in the results of the medical and neuro-psychological tests could be seen (for possible reasons, see above). Therefore at least a <u>chronic</u> mercury intoxication could not be diagnosed on the basis of the blood, urine and/or hair concentration alone, to what values ever the threshold limits are set (see above). An "intoxication" is defined by the presence of the toxin in the body and typical adverse health effects. Deriving from this interpretation we tried to find a balanced result by the combination of mercury concentration in blood, urine and hair and the negative health effects, as summarised in the medical score sum, as described above in detail. The medical test scores were divided in three groups, according to the quartiles (0-25%, 25-75%, 75-100%). Table 6 shows this combination. In principle this means, that the higher the mercury concentration in at least one of the biomonitors was, the lower the number of adverse effects for a positive diagnosis of a mercury intoxication must be and vice versa.

Cases with only moderately elevated mercury levels (i.e. between HBM I and HBM II) are taken for positive, too, if the medical test scores are in the upper quartile region (score sum 10-19).

		Medical Score Sum		
		0-4 5-9 10-19		
Hg in all biomonitors	< HBM I	-	-	-
	> HBM I	-	-	+
Hg at least in one biomonitor	> HBM II	_	+	+
	> BAT	+	+	+

Table 6: Decision for the diagnosis "chronic mercury intoxication"

The case, that a mercury concentration above the occupational threshold limit BAT <u>alone</u> (this means without clinical signs, i.e. medical score 0-4) is responsible for the classification of an intoxication, can be neglected. Only two cases from Mt. Diwata are classified as intoxicated by this.

One case from the control group from Davao exceeded with 31.3 μ g Hg/l blood the BAT-value for metallic and inorganic Hg in blood (25 μ g/l) without any further signs of a mercury intoxication and a medical score sum of 2. It was decided to compare this case to the higher BAT-value of 100 μ g/l blood, as established for organic mercury compounds, because the burden in Davao seems to derive predominantly from organic mercury in sea food. Therefore this case was grouped to be non-intoxicated.

Prevalence of the diagnosis Mercury intoxication

	control	population down- stream	Mt. Diwata without occupational burden	burdened by family members	ball miller	amalgam smelter	other occupation al burdened
total number	42	100	43	20	55	41	6
mercury intoxicated	0	38	10	7	36	35	2
% mercury intoxicated	0%	38.0%	23.3%	35.0%	65.5%	85.4%	33.3%

Table 8: Frequency of a chronic mercury intoxication

By this classification the results from table 8 and figure 15 were obtained. It is striking that nobody from the control group is marked as intoxicated, although the mercury concentration, especially in blood, in this group is in the mean higher than, for instance, in the downstream group. This supports the assumption that the mercury burden of the control group from the coastal population of Davao derives from other mercury species (mainly methyl-mercury from fish) than in the downstream and especially the Mt. Diwata populations. The - in comparison to metallic and inorganic mercury ($25 \mu g/l$) - higher BAT-value in blood for organic mercury compounds (100 $\mu g/l$) shows that in the case of a burden with organic mercury (like methyl-mercury) higher blood concentrations can be tolerated without signs of an intoxication.

<u>Summing up</u>, more than 70% (73 out of 102) of the occupationally burdened population suffer from a chronic mercury intoxication. In the sub-group of amalgam smelter this percentage is even higher (85,4%). From the non occupationally burdened part of the population on and downstream from Mt. Diwata approximately 1/3 (55 from 163) is intoxicated.

Larger differences between the non-occupationally burdened population living on Mt. Diwata and downstream in the plain of Monkayo could not be seen. The differences between persons on Mt. Diwata with and without occupationally burdened family members is relatively negligible, too.

Influence of working conditions

A special investigation was performed on the influence of working conditions on the health of mercury burdened workers.

They were asked

- how they burn amalgam (open or closed)
- how they melt gold (open or closed)
- whether they store mercury at home or at work
- how often they handle with mercury

Striking differences between the three occupationally burdened groups (amalgam burners, ball millers, other Hg workers) in these points could not be seen. Therefore the three groups are pooled together to get one larger Hg burdened group of 102 participants for this statistical evaluation.

Moreover it was found that the answers to the points "amalgam burning" and "gold melting" correspond highly significant. This means that these two terms are interchangeable. The mercury concentration in blood, urine or hair do not differ significantly between workers, burning amalgam in open or closed vessels (Mann-Whitney-U-test). As expected, the same result was achieved for gold melting. In contrast to this, the medical score sum (established as shown in table 4) was significantly higher in the group of workers, which burned amalgam or smelted gold in open vessels in contrast to those who did this in a closed system (see figure 16). A higher medical score means a worse health condition. Consequently a mercury intoxication was diagnosed in 77.6% of the 76 workers, which burned amalgam in open vessels, while "only" 53.8% of the 26 workers, which indicate that they burned amalgam in closed systems are intoxicated. For gold melting almost equal results were obtained (79.2%/48.0%). These results evidently show how urgently necessary a higher acceptance for closed systems for burning amalgam or smelting gold for the workers themselves is.

The parameter "storage of mercury at home or at work" do not interrelate with the former two parameters of amalgam burning or gold melting in open or closed vessels. Therefore this parameter can be analysed separately. The result was similar: No influence on the mercury concentration in blood, urine or hair, but again on the medical sore sum. It was both significantly higher (i.e. the health conditions were worse) in the groups, which stored mercury either at home or at work in comparison to workers, which did not do this. The frequency of the diagnosis "mercury intoxication" tends to higher values in the storing groups, too. This shows that the careless storage of liquid mercury at home or at work is a further parameter for the high mercury burden not only for the environment (and from this indirectly of people, living in this area) but directly for the workers which handle this toxic substance.

The frequency of handling mercury do not correlate to any of the parameters as tested above. This shows that not the frequency but the care at the handling of liquid mercury is the crucial point.

31

Influence on Pregnancy

One major problem of mercury is a possibly adverse effects on the growing foetus due to a maternal burden and a cross of mercury through the placenta. High numbers of miscarriages, stillbirths and birth defects have been reported as consequence of the mass intoxication with mercury in Minamata, Japan, 1956 or the Iraq, 1972/73 (Drasch 1994).

	Sub-group			
	control	downstream	Mt. Diwata	
No of mothers	10	38	32	
Total no. of pregnancies	34	203	124	
mean no. of pregnancies	3.4	5.3 **	3.9	
mean no of miscarriages or still birth	0.50	0.61	0.53	
mean no. of children, died after birth	0.30	0.08	0.25	
no. of children with birth defects	0	0	2 (1 clubfoot, 1 heart defect)	

Table 9: Problems with pregnancies, as reported by the mothers.

This study was not primarily designed to detect possible adverse effects on the foetus, but as a side result some data were obtained to this complex and should be therefore discussed.

80 females (10 controls from Davao, 38 from the downstream area of Monkayo and 32 from Mt. Diwata) reported a total of 361 pregnancies (1-13). Table 9 shows the statistical evaluation of the data.

The mean number of children per mother on Mt. Diwata was similar to the control group, while in the downstream group it was significantly higher. The frequency of miscarriage, stillbirth or babies, dies after birth are similar or even lower in the mercury burdened groups. For the control and the downstream group no birth defect was reported. Two birth defects were noted on Mt. Diwata: one with a clubfoot and one with a heart defect. Beside the fact that these numbers are too low for a statistical evaluation, these two reported birth defects are <u>not</u> characteristic for a damage of the foetus by metallic, inorganic or organic mercury compounds, as reported e.g. from the mass catastrophes of Minamata or the Iraq. In summary, a negative effect of the mercury burden in Mindanao on the foetal development could not be proved. But qualifying it must be considered for this statement that the number of cases was too low for a final conclusion and this study was primarily not designed to detect such an effect. Special studies on this topic, as started 1997 in the area of Apokun, near to Mt. Diwata, by Ramirez and co-workers (1999), should urgently continued and implemented on Mt. Diwata, too.

Conclusions (Gustav Drasch. Stephan Böse-O'Reilly)

Health problems around Mt Diwata, not related to mercury

At the moment it does not seem to be acceptable that **children** live in Diwalwal. Crime and accidents related to illegal mining activities, missing law and order in the area, as well as child work in physically and environmentally health threatening jobs are not suitable for the healthy development of a child. Missing sanitary standards and high exposure to mercury are further reasons to consider.

The **occupational related health risk** of mining has to be properly assessed (tuberculosis, ventilation, accidents). One first step to reduce the health hazards in Diwalwal might be a proper **zoning** into industrial areas, commercial areas and housing areas.

Mercury as a severe health hazard

A major part of the tested participants in Monkayo and Diwalwal has an elevated internal mercury burden, which exceeds in many cases toxicological threshold limits. Ball-mill workers and amalgam smelters have in 55% respectively 61% mercury levels above toxicological threshold limits (HBM II). Approximately 20% of both groups exceed even the high occupational threshold limit, as valid in Germany (BAT-value).

Participants from Monkayo, which are "only" exposed by an environmental pathway, but not occupationally, do exceed in 26% the HBM II-threshold limit.

The Hg-burden in the control group in Davao is as well fairly high (19,5% > HBM II).

Symptoms, typical for a especially chronic mercury intoxication, are correlated on a very high significance level to the mercury burden defined by residence and/or occupation. Mercury levels are as well correlated on the same level of significance with the different pathways of mercury burden of the participants.

Chronic mercury intoxication was diagnosed by a defined combination of typical symptoms with mercury levels in the biomonitors (blood, urine, hair). An intoxication had to be diagnosed in a high percentage of the population in the Mt. Diwata area, e.g. ball-mill workers in approximately 65% and amalgam smelters in 85%. To a lesser but still not acceptable extent (approximately 33%) mercury intoxication was found in the non occupationally exposed population on Mt. Diwata and downstream in the plain of Monkayo (38%). No mercury intoxication was found in the control area of Davao.

Further investigations, which still will be performed with the specimen achieved for this study

As far as possible a **speciation in inorganic and organic mercury** in the collected blood, urine and hair samples will be performed for scientific purpose. The results will give further information on the distribution and predominance of mercury species in the different sub-groups. From this more information can be obtained e.g. on questions, like:

- Is the population on Mt. Diwata (especially the non occupationally involved) and the population downstream in the plain of Monkayo predominantly burdened by metallic or inorganic mercury or by mercury, methylated in the aquatic food chain?
- Where derives the unexpected high mercury burden in the control group of Davao from?

A better risk assessment for the different populations and better suggestions for an effective harm reduction will be obtained from this data.

Mercury intoxication treatment

Mercury is a considerable health hazard in the area of Monkayo and Mt. Diwata (Mt. Diwalwal). **It is not a rare health hazard, it is an epidemic disease**. Mercury intoxication is epidemic in occupationally exposed workers, but it is also epidemic in the "only" environmentally exposed population. Therefore it is urgently necessary to reduce the severe symptoms of chronic mercury intoxication, as manifested especially in the central and peripheral nervous system and in the kidney.

In any case of an intoxication the first step must be a stop of exposure to the harmful toxin. Therefore mercury exposure has to be stopped or at least drastically reduced urgently in this area. This means a stop or a dramatic reduction in the use of mercury for the extraction of gold from the ore by the amalgamation technique. Considerable effort has urgently to be taken, to improve these working habits. Amalgam burning and gold melting in closed vessels is essential for a reduction of the mercury burden. A safer storage and handling of liquid mercury is urgently necessary, too.

Moreover, the environmentally important pathways of mercury down from Mt. Diwata to the basin of Monkayo should be investigated - whether it is with water, sediment, air or food. If a stop or reduction of mercury exposure is not carried out within the near future, any medical treatment can only be of a short time efficiency, since by re-exposure a re-intoxication is more than likely.

The medical treatment of the intoxicated participants should be performed with a newer chelating agent (detoxificant), like DMSA (Dimercaptosuccinic acid) or DMPS (Dimercaptopropanesulfonic acid) (Aaseth 1995). While DMSA is more common in Russia and Eastern European Countries, DMPS was introduced in Germany by the Bundesinstitut für Arzneimittel (former Bundesgesundheitsamt) especially for the treatment of mercury intoxication. In humans, DMPS is an effective mobilising agent for mercury (for reviews see e.g. Aposhian 1995 or Aaseth 1995). Compared to previously used antidotes such as BAL (Dimercaprol), DMPS has many advantages, such as less toxicity and (especially necessary for an application in field) the possibility of an <u>oral</u> application. More is known about the pharmacokinetetics of DMPS in human than about any other dimercapto chelating agent, including DMSA (Aaseth

36

1995, Gonzalez-Ramirez 1998). An other possible antidote, D-Penicillamin, is much less effective (Cichini 1989)

Since, from the medical results, it seems very likely that the neurological symptoms are predominant (like tremor), it has to be doubted to which extent the severe symptoms of the chronic mercury intoxication can still be treated at all. It must be taken into consideration that, as in the case of stroke patients or severe brain damaged patients due to accidents, neuronal tissue, for example the brain, is the only tissue of the body, that can not be replaced after neuronal cell damage. Moreover it is questionable whether DMPS can transport mercury to a relevant extent out of the brain tissues through the lipophilic brain-blood-barrier. A better prognosis can be given for the reversibility of a mercury induced damage of the kidney by a DMPS treatment.

Chelating treatment can lower the body burden with mercury, but not in any case it may succeed in a full recovery from symptoms. So it is of even more importance, to stop any further mercury burden of the population on and around Mt. Diwata.

Suggestions

Medical treatment

Judging the possible benefits, risks and (even if not very ethically:) costs of a treatment with a chelating agent, at least an attempt for such a medical treatment is to recommend indisputably. This should be started as soon as possible. But it must be done under a scientific study design, to be able to evaluate both the extent of reduction of the internal mercury burden and of mercury related symptoms. It must be kept in mind that, up to now, there are no comparable studies published in the international literature on the treatment of a population in this order of magnitude, especially in a region of the third world, and chronically intoxicated by a mixture of different mercury species (metallic, inorganic, organic), with total different toxicodynamic and toxico-kinetic properties. In principle, we suggest to treat <u>all</u> participants of the present study, found to be mercury intoxicated (max. 128, with the exception of few small children) by the following regime:

- first a medical and neurological check with methods, which has been proved in this study to be effective for the diagnosis of a mercury burden. And one blood and urine sample before the treatment to get a basis value.
- Treatment for 14 days with DMPS sodium salt capsules (Dimaval[®] Heyl or Mercuval[®] biosyn) orally, 200-300-400 mg per day (according to body weight), in two divided doses (morning and evening), administered by a nurse.
- One urine sample 3-5 hours after the first treatment, to get information on the increase of mercury in urine after DMPS ("DMPS-test").
- Blood and urine samples one day after finishing the treatment and a second medical and neurological check after the treatment, to determine the decrease of mercury in the body fluids by the treatment and to diagnose a possible improvement of the health status by the treatment.

Some selected participants from Mt. Diwata and Monkayo should deliver urine samples during the whole treatment period of 14 days once a day, taken again 3-5 hours after the intake of the DMPS capsules in the morning. From the (decreasing) mercury concentrations in these urine samples it could be calculated, how long a treatment is necessary (one or two weeks?), a question, which is still unanswered in literature (Gonzalez-Ramirez 1998). The result seems to be of considerable interest for a recommendation of a further treatment of similar populations especially under similar difficult conditions in the third word in the future, because:

- DMPS may show undesirable side effects, which are relatively rare, if the drug is given orally, but increase with the time of treatment.
- DMPS sweeps not only mercury, but also essential trace elements like copper out

of the body.

- the shorter the treatment can be limited, the greater is the compliance that the drug will be really taken by the ill subjects without medical administration.
- DMPS, as traded in Germany, is a relatively expensive drug.

A more complicated regime (e.g. with 3 cycles of treatment for 8 days and treatment free intervals of 5 days, as proposed by Gonzalez-Ramirez et al. (1998) will not work under adverse field conditions like on Mt. Diwata.

A treatment of small children with DMPS is not proved enough that it can be recommended, especially under conditions like in this area.

Suggestions for a treatment study in detail will be presented immediately.

Further Suggestions

Beside this, to diagnose and to treat mercury intoxication in the future in the area of Monkayo and Mt. Diwata we would suggest to implement:

- Training programmes for the Monkayo health centre and other health centres in the area
- Clinical training including a standardised questionnaire and examination flow scheme
- Laboratory equipment within the area to be able to test for mercury in human specimens (urine, blood)
- Treating facilities, including standardised recommendations for treatment, financial aspect of treatment, legal problem of importing drugs like DMPS to the Philippines

- Assessment of the amount of mercury already existing in the biosphere. Since the local people eat up to three times daily fish and fish is known to be a mayor source of mercury intake, we would suggest to assess the mercury burden of local fish and all the fish along the Aguasan river system down the bay of Butuan. Also the assessment of mercury in the local chickens, pigs and fruit plants in Diwalwal and in rice and other crops irrigated by Naboc and Mamunga river water, is recommended.
- Assessing in a different study design the possibility of mercury related birth defects, increased abortion/miscarriage rates, infertility problems, learning difficulties in childhood or other neuro-psychological problems related to mercury exposure.

Literature:

Aaseth J, Jacobsen D, Andersen O, Wickstrom E (1995) Treatment of mercury and lead poisoning with dimercaptosuccinic acid and sodium dimercaptopropane-sulfonate: A review. Analyst 120, 23-38

Achmadi UF (1994) Occupational exposure to mercury at the gold mining: a case study from Indonesia. In: Environmental mercury pollution and its health effects in Amazon River Basin. National Institute Minamata Disease and Inst. Biophysics of the University Federal do Rio de Janeiro. Rio de Janeiro, pp 10-16

Akagi H et al (1994) Methylmercury pollution in Tapajós River Basin, Amazon. Environ Sci 3, 25-32

Akagi H, Castillo E, Maramba N, Francisco AT (1999) Health assessment for mercury exposure among children residing near a gold processing and refining plant.
Proc. of the Int Conference Mercury as a Global Pollutant, Rio de Janeiro, Brazil, p.
421

Aposhian HV et al (1995) Mobilization of heavy metals by newer, therapeutically useful chelating agents. Toxicology 97, 23-38

Barbosa AC et al (1995) Mercury contamination in the Brazilian Amazon. Environmental and occupational aspects. Water Air Soil Pollut 80, 109-121

Boischio AAP, Henshel D, Barbosa AC (1995) Mercury exposure through fish consumption by the upper Madeira River population, Brazil. Ecosyst Health 1,177-192

Branches FJP, Erickson T, Aks SE, Hryhorczuk DO (1993) The price of gold: mercury exposure in the Amazon Rain Forest. J Clin Toxicol 31, 295-306

Câmara VM (1994) Epidemiological assessment of the environmental pollution by mercury due to gold mining in the Amazon River Basin. In: Environmental mercury pollution and its health effects in Amazon River Basin. National Institute Minamata

Disease and Inst. Biophysics of the University Federal do Rio de Janeiro. Rio de Janeiro, pp 80-84

Castro MB, Albert B, Pfeiffer WC (1991) Mercury levels in Yanomami indians hair from Roraima, Brazil. Proceedings 8th Int. Conference Heavy metals in the environment. Edinburgh 1, 367-370

Castillo ES, Maramba NFC, Akagi, H, Francisco-Rivera ATT (1999) Quality assurance of blood mercury levels among schoolchildren exposed to elemental mercury in Apokon, Tagum, Davao del Norte, Philippines, 1998. Proc. of the Int Conference Mercury as a Global Pollutant, Rio de Janeiro, Brazil, p. 422

Cichini G et al (1989) Effekt von DMPS und D-Penicillamin bei inhalativer Intoxikation mit metallischem Quecksilber. Intensivmed Notf Med 26, 303-306

Cleary D et al. (1994) Mercury in Brazil. Nature, 613-614

Davidson PW et al (1998) Effects of prenatal and postnatal merthylmercury exposure from fish consumption on neurodevelopment. J Am Med Assoc 280, 701-707

Deutsche Forschungsgemeinschaft (ed) (1999) MAK- und BAT-Werte-Liste 1999. VCH-Verlagsgesellschaft, Weinheim, Germany

Drasch G (1994): Mercury. In: Seiler HG, Sigel A, Sigel H (eds.): Handbook on metals in clinical and analytical chemistry. New York: Marcel Dekker, 479-494.

Drasch G et al. (1997) Are blood, urine, hair, and muscle valid bio-monitoring parameters for the internal burden of men with the heavy metals mercury, lead and cadmium? Trace Elem Electrolytes 14, 116-123

Florentine MJ, Sanfilippo DJ (1991) Elemental mercury poisoning. Clin Pharm 10, 213-221

Forsberg BR et al. (1994) High levels of mercury in fish and human hair from the Rio Negro basin (Brazilian Amazon): natural background or anthropogenic. In: Environmental mercury pollution and its health effects in Amazon River Basin. National Institute Minamata Disease and Inst. Biophysics of the University Federal do Rio de Janeiro. Rio de Janeiro, pp 33-39

Gonzalez-Ramirez et al (1998) DMPS (2,3-Dimercaptopropane-1-sulfonate, Dimaval) Decreases the Body Burden of Mercury in Humans Exposed to Mercurous Chloride. J Pharmacol Exp Therap 287, 8-12

Grandjean P et al (1997) Cognitive deficit in 7-year-old children with prenatal exposure to methylmercury. Neurotoxicol Teratol 19,417-428

Grandjean P et al (1999) Methylmercury Neurotoxicity in Amazonian Children Downstream from Gold Mining. Environ Health Perspect 107, 587-591

Kijewski H (1993) Die forensische Bedeutung der Mineralstoffgehalte in menschlichen Kofhaaren. Schmidt Römhild Verlag, Lübeck, Germany

Kommission Human-Biomonitoring des Umweltbundesamtes Berlin - Institut für Wasser-, Boden- und Lufthygiene des Umweltbundesamtes (1999) Stoffmonographie Quecksilber - Referenz- und Human-Biomonitoring-Werte (HBM). Bundesgesundheitsblatt: 42:522-532.

Krause C et al (1996) Umwelt-Survey 1990/92, Studienbeschreibung und Human-Biomonitoring. Umweltbundesamt Berlin, Germany (ed.)

de Lacerda L, Salomons W (1998) mercury from Gold and Silver Mining: A Chemical Time Bomb? Springer, Berlin, Heidelberg

Lockowandt O (1996) Frostigs Entwicklungstest der visuellen Wahrnehmung. Weinheim: Beltz

Malm O, Pfeiffer WC, Souza CMM, Reuther R (1990) Mercury pollution due to gold mining in the Madeira River Basin, Brazil. Ambio 19,11-15

Malm O et al (1995a) Mercury and methylmercury in fish and human hair from Tapajós River Basin, Brazil. Sci Tot Environ 175, 127-140

Malm O et al (1995b) An assessmant of Hg pollution in different gold mining areas, Amzon, Brazil. Sci Tot Environ 175, 141-150

Masur H, Papke K, Althoff S, Oberwittler C (1995) Skalen und Scores in der Neurologie. Thieme, Stuttgart

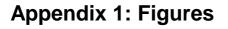
Ramirez GB, Vince Cruz CR, Pagulayan O, Ostrea E, Dalisay C (1999) The Tagum study I: Mercury levels in mother's blood, transitional milk, cord blood, baby's hair and meconium. Pediatrics, submitted for publication

WHO (1980) Recommended health based limits in occupational exposure to heavy metals. Technical Series Report No 647, Geneva

WHO (1991) Environmental Health Criteria 118: Inorganic Mercury. Geneva

Wilhelm M (2000): Quecksilber In Böse-O'Reilly S, Kammerer S, Mersch-Sundermann V, Wilhelm M: Leitfaden Umweltmedizin, 2. Auflage. Urban und Fischer, München

Zimmer R, Volkamer M (1984) MOT - Motoriktest. Beltz, Weinheim



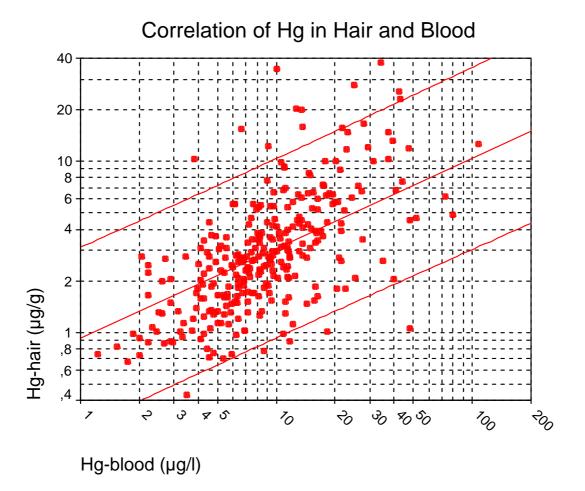
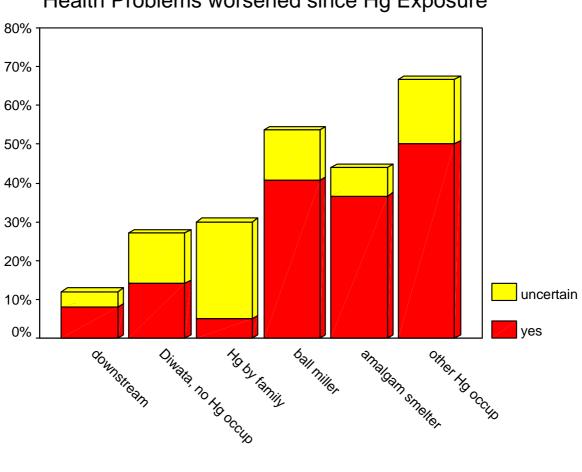
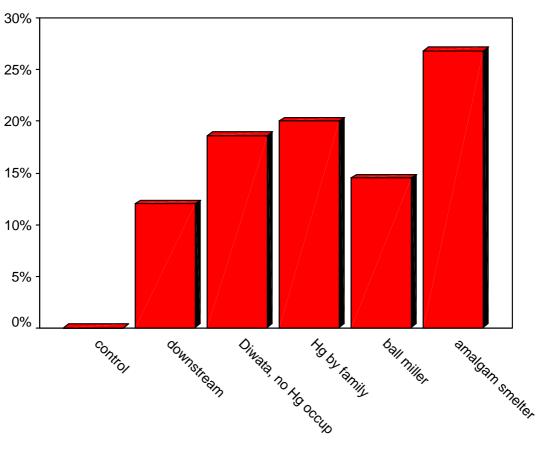


Figure 1: Correlation of Mercury in hair and blood. The line in the middle represents the regression line, the two border lines the 90% confidence interval for the individual values (i.e. 90% of all values are within these two lines.



Health Problems worsened since Hg Exposure

Figure 2: Health problems worsened since mercury exposure



Prevalence of Ataxia

Figure 3: Prevalence of ataxia

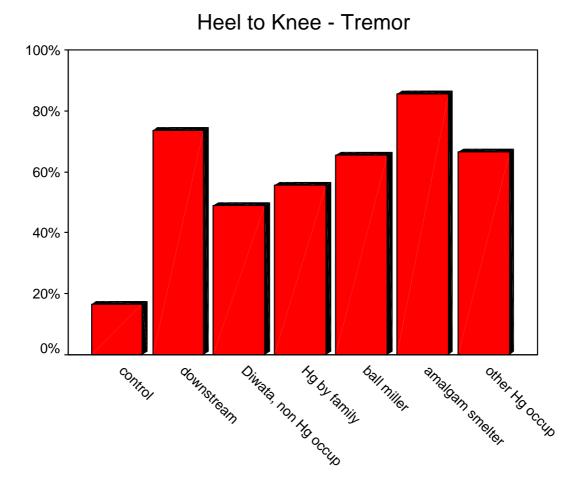


Figure 4 : Prevalence of heel to knee tremor

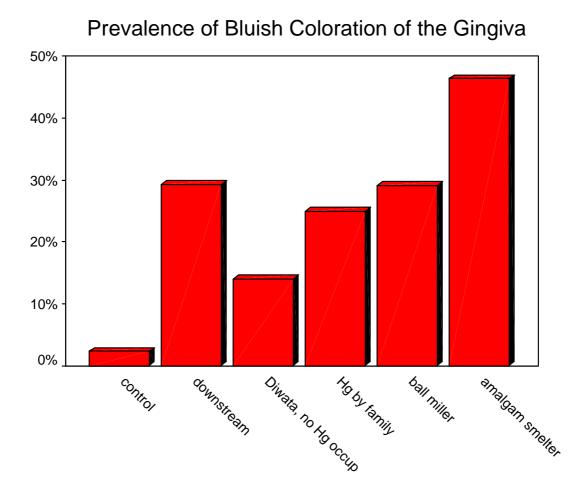
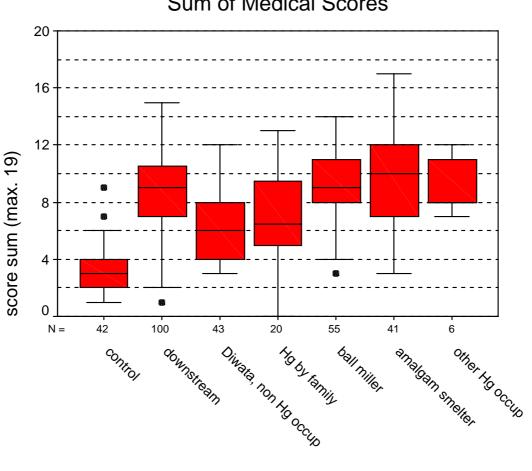


Figure 5: Prevalence of bluish discoloration of the gingiva



Sum of Medical Scores

Figure 6: Sum of medical scores (for details of calculation see text)

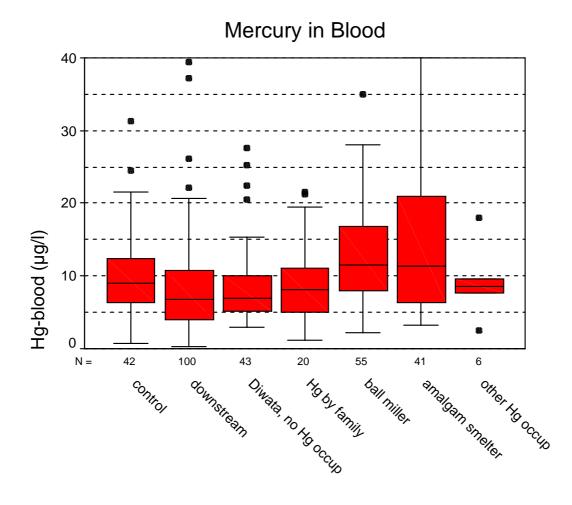


Figure 7: Box plots of mercury in blood

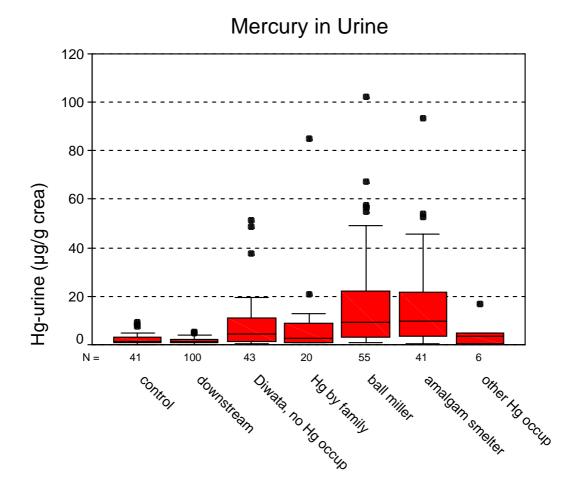


Figure 8: Box plots of mercury in urine

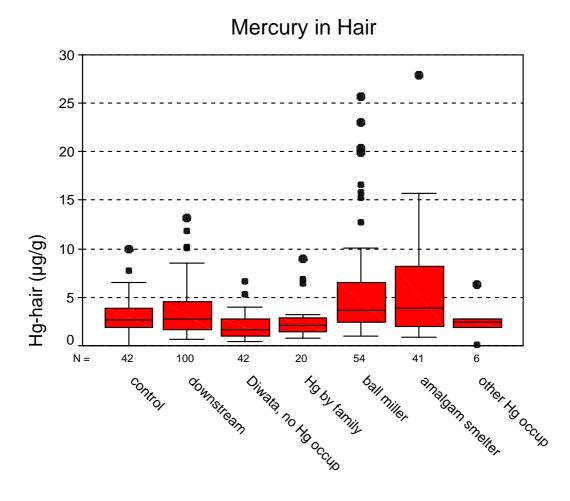


Figure 9: Box plots of mercury in hair

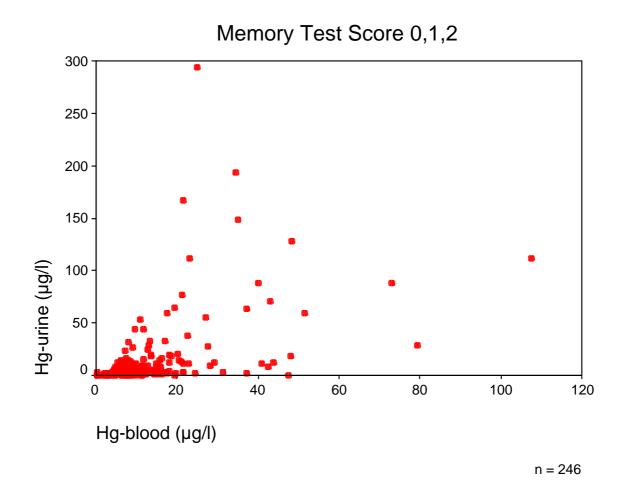


Figure 10: Scatter-plot of mercury blood and urine concentration of participants with a below-average (0 points) to average (1,2 points) result in the memory test

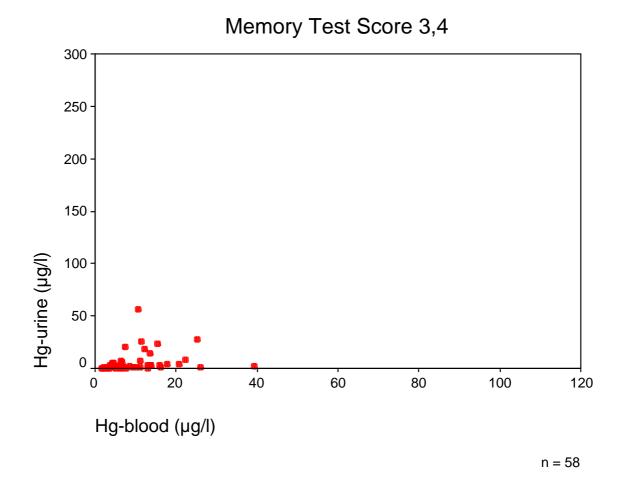
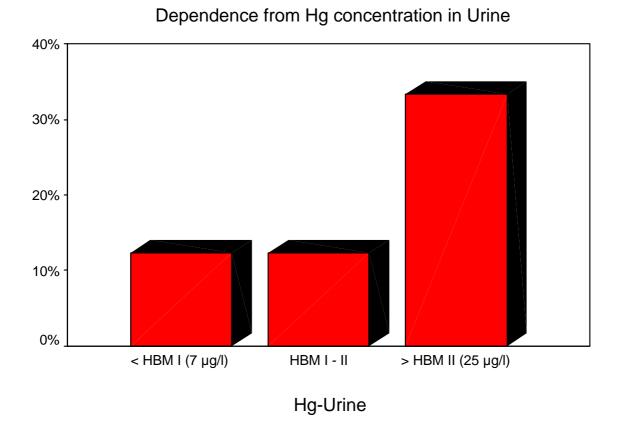


Figure 11: Scatter-plot of mercury blood and urine concentration of participants with an above-average (3,4 points) result in the memory test



Frequency of Proteinuria

Figure 12: Frequency of Proteinuria, depending on the mercury concentration in urine (HBM = human biomonitoring value, explanation see text)

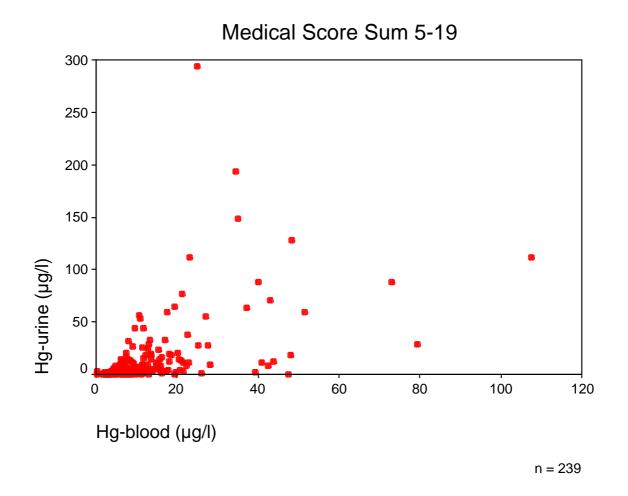


Figure 13: Scatter-plot of mercury blood and urine concentration of participants with an average to below-average (5 -19 points) medical score sum

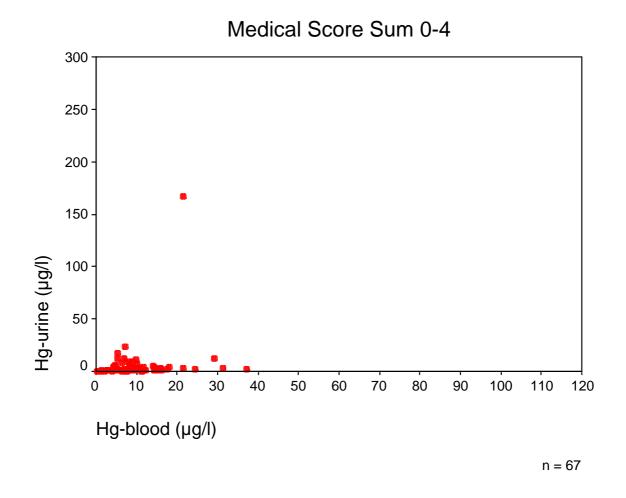


Figure 14: Scatter-plot of mercury blood and urine concentration of participants with an above-average t (0 - 4 points) medical score sum

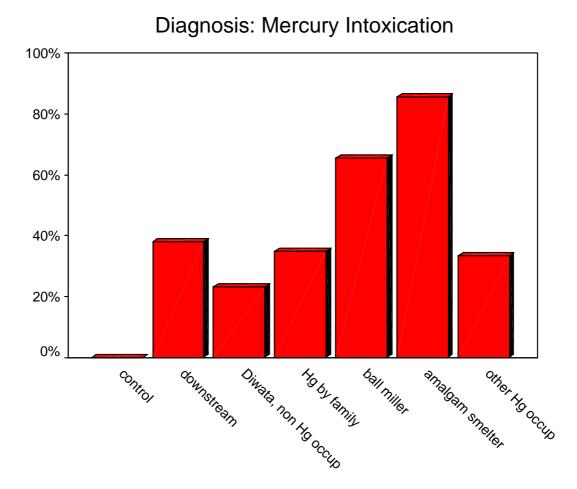


Figure 15: Prevalence of the diagnosis "mercury intoxication" in the different populations

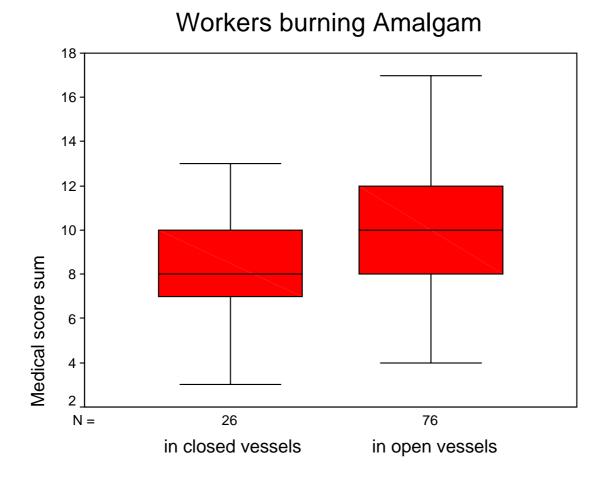


Figure 16: Medical score sum of workers, burning amalgam in closed or open vessels (The higher the medical score sum is, the worse is the health condition).

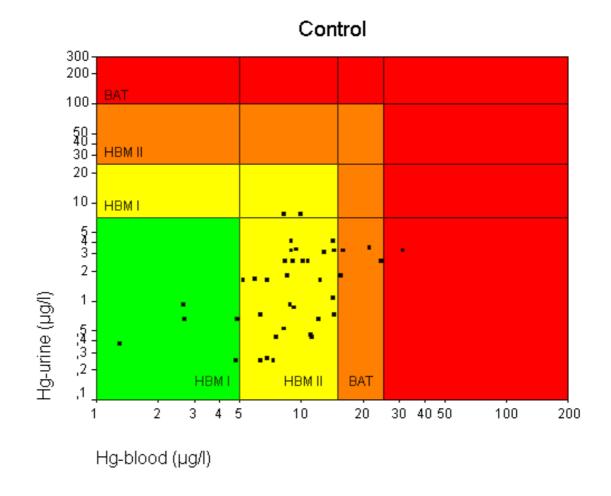
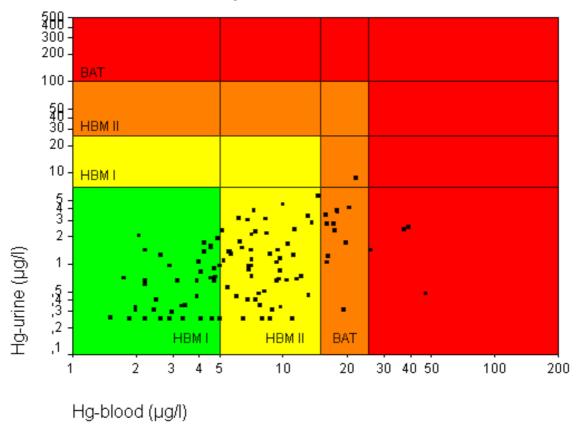
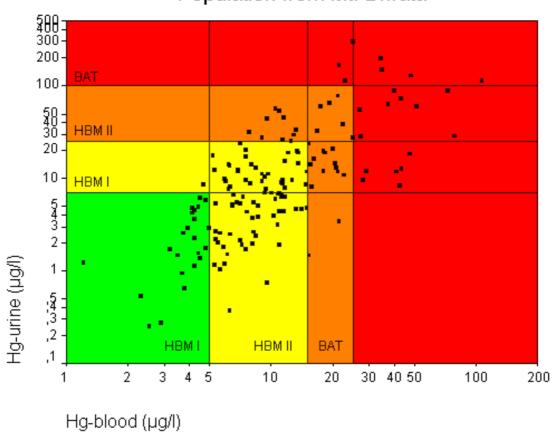


Figure 17: Prevalence of exceeding toxicologically defined threshold limits (HMB I, HMB II, BAT) in the control group from Davao



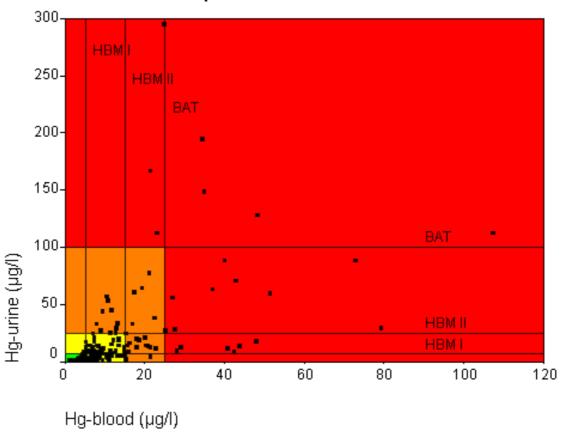
Population downstream

Figure 18: Prevalence of exceeding toxicologically defined threshold limits (HMB I, HMB II, BAT) in the population living downstream in the plain of Monkayo



Population from Mt. Diwata

Figure 19: Prevalence of exceeding toxicologically defined threshold limits (HMB I, HMB II, BAT) in the population living on Mt. Diwata (occupational burdened and non-burdened)



Population from Mt. Diwata

Figure 20: Same scatter plot as in figure 19, but both axis on a linear scale

Appendix 2: Table 3

signifi- cance	Data or Test	Value or score	not ccupational burdened				occupational burdened			
			control	down- stream	Mt. Diwata	by family member	ball miller	smelter	other occup.	
	case number		42	100	43	20	55	41	6	
	Anamnestic data:									
***	alcohol	0/1	9.5%	14.0%	9.3%	0%	27.3%	22.0%	50.0%	
***	metallic taste	0/1	0%	22.2%	11.6%	10.5%	45.5%	31.7%	33.3%	
***	salivation	0/1	0%	20.2%	11.6%	31.6%	38.2%	36.6%	16.7%	
***	tremor at work	0/1	2.4%	3.0%	9.3%	10.5%	12.7%	31.7%	16.7%	
***	sleeping problems	0/1	0%	8.0%	14.0%	5.0%	40.7%	36.6%	50.0%	
***	health problems worsened since Hg exposed		11.9%	36.0%	16.7%	40.0%	56.4%	36.6%	33.3%	

signifi- cance	Data or Test	Value or score	not ccupational burdened				occupational burdened			
			control	down- stream	Mt. Diwata	by famil membe	•	smelter	other occup.	
	Clinical data:									
***	bluish coloration of gingiva	0/1	2.4%	29.3%	14.0%	25.0%	29.1%	46.3%	33.3%	
*	rigidity of gait	0/1	0%	6.0%	2.3%	15.0%	12.7%	9.8%	0%	
***	ataxia of gait	0/1	0%	12.0%	18.6%	20.0%	14.5%	26.8%	50.0%	
-	ataxia of posture	0/1	69.0%	81.0%	67.4%	68.4%	34.5%	90.2%	100.0%	
-	tremor with posture holding	0/1	81.0%	81.0%	79.1%	83.3%	45.5%	65.9%	83.3%	
-	Rhomberg standing test	0/1	95.3%	91.0%	88.4%	88.9%	83.7%	97.5%	100.0%	
***	finger to nose tremor	0/1	14.3%	31.0%	23.3%	11.1%	21.8%	26.8%	50.0%	
-	finger to nose ccordination	0/1	33.3%	38.0%	23.3%	16.7%	25.5%	39.0%	50.0%	
***	dysdiadochokinesis	0/1	23.8%	46.0%	27.9%	25.0%	54.5%	61.0%	66.7%	
*	tremor of tongue	0/1	75.6%	94.0%	86.0%	65.0%	81.8%	87.8%	83.3%	
-	salivation	0/1	0%	1.0%	0%	0%	3.6%	2.4%	0%	

signifi- cance	Data or Test	Value or score	not ccupational burdened				occupational burdened			
			control	down- stream	Mt. Diwata	by family member	ball miller	smelter	other occup.	
	Clinical data (continued):									
-	dysathria	0/1	0%	1.0%	0%	0%	3.5%	0%	0%	
-	pouring	0/1	71.3%	75.0%	79.1%	77.8%	52.7%	75.6%	83.3%	
-	field of vision	0/1	0%	3.0%	0%	0%	11.1%	0%	0%	
-	nystagmus	0/1	59.5%	44.0%	44.2%	15.0%	54.5%	61.0%	83.3%	
***	heel to knee ataxia	0/1	16.7%	58.6%	44.2%	38.9%	61.8%	73.2%	66.7%	
***	heel to knee tremor	0/1	16.7%	73.7%	48.8%	55.6%	65.5%	85.4%	66.7%	
*	PSR test	0/1	4.8%	9.0%	9.3%	5.0%	10.9%	26.8%	33.3%	
*	BSR	0/1	28.6%	38.0%	32.6%	15.0%	34.5%	46.3%	50.0%	
-	Babinski	0/1	2.4%	0%	2.3%	0%	5.5%	2.4%	16.7%	
***	sucking	0/1	16.7%	45.0%	32.6%	25.0%	36.4%	41.5%	66.7%	
-	sensory	0/1	0%	6.1%	0%	0%	3.7%	7.3%	16.7%	
*	proteinuria	0/1	4.8%	16.0%	9.3%	0%	21.8%	24.4%	0%	

signifi- cance	Data or Test	Value or score	not ccupational burdened				occupational burdened			
			control	down- stream	Mt. Diwata	by family member	ball miller	smelter	other occup.	
	Neuro- psychological test									
***	memory test	0	40.5%	11.1%%	18.6%	5.6%	20.0%	14.6%	0%	
		1,2	57.1%	47.5%	67.4%	94.4%	67.3%	80.5%	83.3%	
		3,4	2.4%	41.4%	14.0%	0%	12.7%	4.9%	16.7%	
***	match box test	11-15 sec	47.6%	15.2%	37.2%	22.2%	14.8%	14.6%	33.3%	
		16-20 sec	47.6%	54.5%	48.8%	55.6%	55.6%	53.7%	66.7%	
		21-36 sec	4.8%	30.3%	14.0%	22.2%	29.6%	31.7%	0%	
***	Frostig test	13-16	57.1%	15.2%	11.9%	11.1%	29.1%	34.1%	0%	
		10-12	33.3%	46.5%	52.4%	55.6%	38.2%	34.1%	66.7%	
		3-9	9.5%	38.4%	35.7%	33.3%	32.7%	31.7%	33.3%	

signifi- cance	Data or Test	Value or score	not ccupational burdened				occupational burdened			
			control	down- stream	Mt. Diwata	by family member	ball miller	smelter	other occup.	
	Neuro- psychological test (continued)									
***	pencil tapping test	65-78	47.6%	20.2%	39.5%	0%	12.7%	22.0%	66.7%	
		54-64	50.0%	50.5%	41.9%	61.1%	58.2%	51.2%	33.3%	
		23-53	2.4%	29.3%	18.6%	38.9%	29.1%	26.8%	0%	
***	Medical test score	median	3	9	6	6.5	9	10	8	
		0-4	76.2%	12.0%	30.2%	15.0%	9.1%	4.9%	0%	
		5-9	23.8%	47.0%	53.5%	60.0%	41.8%	34.1%	66.7%	
		10-21	0%	41.0%	16.3%	25.0%	49.1%	61.0%	33.3%	

signifi- cance	Data or Test	Value or score	not ccupational burdened				occupational burdened				
			control	down- stream	Mt. Diwata	by family member	ball miller	smelter	other occup.		
	Biomonitoring										
***	Hg-blood	median	9.0µg/l	6.8µg/l	6.9µg/l	8.7µg/l	11.5µg/l	11.4µg/l	8.6µg/l		
		> HBM II	11.9%	15.0%	11.6%	20.0%	29.1%	39.0%	16.7%		
		> BAT	2.4 %	4.0%	4.7%	0%	21.8%	14.6%	0%		
		max.	31.3µg/l	47.5µg/l	27.6µg/l	21.5µg/l	107.6µg/l	43.8µg/l	18.0µg/l		
***	Hg-urine (µg/l)	median	1.0µg/l	5.6µg/l	1.3µg/l	9.4µg/l	17.6µg/l	13.1µg/l	4.0µg/l		
		> HBM II	0%	0%	7.0%	5.0%	23.6%	31.7%	0%		
		> BAT	0%	0%	0%	0%	5.5%	9.8%	0%		
		max.	7.6µg/l	8.6µg/l	37.7µg/l	76.4µg/l	148.0µg/l	294.2µg/l	12.1µg/l		
***	Hg-urine (µg/g crea)	median	1.4µg/g	1.4µg/g	4.4µg/g	2.8µg/g	7.9µg/g	9.8µg/g	3.6µg/g		
		> HBM II	0%	0%	7.0%	10.0%	30.9%	29.3%	0%		
		max.	9.3µg/g	5.2µg/g	51.4µg/g	85.1µg/g	196.3µg/g	93.3µg/g	16.9µg/g		

signifi- cance	Data or Test	Value or score	not ccupational burdened				occupational burdened			
			control	down- stream	Mt. Diwata	by family member	ball miller	smelter	other occup.	
	Biomonitoring									
***	Hg-hair	median	2.65µg/g	2.77µg/g	1.63µg/g	2.09µg/g	3.62µg/g	3.92µg/g	2.40µg/g	
		> 5 µg/g	11.9%	23.0%	4.8%	15.0%	33.3%	41.5%	16.7%	
		max.	34.71µg/g	13.17µg/g	6.60µg/g	8.91µg/g	25.63µg/g	37.76µg/g	6.29µg/g	
***	blood or urine or hair	> HBM II	19.5%	26.0%	14.3%	30.0%	55.5%	61.0%	16.7%	
***	blood or urine	> BAT	2.4%	4.0%	4.7%	0%	21.8%	19.5%	0%	
	Diagnosis									
***	Hg intoxication	case no.	0	38	10	7	36	35	2	
		%	0%	38.0%	23.3%	35.0%	65.5%	85.4%	33.3%	