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Mercury exposure and malaria prevalence among gold miners in Pará, Brazil

Exposição a mercúrio e prevalência de malária entre garimpeiros de ouro do Pará, Brasil

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Abstract *Economic development, including resource extraction, can cause toxic exposures that interact with endemic infectious diseases. Mercury is an immunotoxic metal used in the amalgamation of gold, resulting in both occupational exposures and environmental pollution. A cross-sectional medical survey was conducted in 1997 on 135 garimpeiros in Para, Brazil, because of their risks of both mercury exposure and malaria transmission. Mean levels of blood and urine mercury were well above non-exposed background levels. Twenty-six subjects had malaria parasitemia: Health symptoms consistent with mercury exposure were reported, but neither symptoms nor signs correlated with mercury levels in blood or urine. We did not find a dose response relationship between mercury exposure and likelihood of prevalent malaria infection, but there was a possible reduction in acquisition of immunity that may be associated with conditions in gold mining, including mercury exposure.*

Key-words: Mercury. Garimpagem. Malária. Toxicity.

Resumo *O desenvolvimento econômico, incluindo extração de recursos naturais, pode causar exposições tóxicas que interagem com doenças infecciosas endêmicas. O mercúrio é um metal imunotóxico usado na amalgamação do ouro, resultando em exposição ocupacional e poluição ambiental. Devido aos riscos da exposição ao mercúrio e transmissão de malária em 135 garimpeiros do Pará, Brasil, uma avaliação médica "cross-sectional" foi conduzida em 1997. Níveis médios de mercúrio no sangue e na urina encontram-se bem acima dos níveis basais daqueles não expostos. Vinte e seis indivíduos apresentaram parasitemia de malária; sintomas relacionados com exposição ao mercúrio foram adquiridos, mas nenhum dos sintomas/sinais está correlacionado com níveis de mercúrio no sangue ou na urina. Não foi encontrada nenhuma relação de dose-resposta entre exposição ao mercúrio e provável infecção de malária prevalente. Entretanto, verificou-se uma possível redução na aquisição de imunidade que talvez esteja relacionada às condições de garimpagem, incluindo exposição ao mercúrio.*

Palavras-chaves: Mercúrio. Garimpagem. Malária. Toxicidade.

During processes of development and resource extraction, populations in many developing countries are increasingly being exposed to chemical pollutants, while exposure to endemic infectious diseases continues. Thus, uncontrolled development may add to their disease burden by altering host exposures and/or susceptibility to infection. The impacts of global and local environmental change on infectious disease has

been understood mainly in terms of population density and the distribution of pathogens and their vectors^{1 24 34}. For example, temporal increases in malaria incidence in Rwanda²² and Colombia⁴ have been associated with the effects of periodic El Niño events and overall surface warming on vector thermosensitivity. No studies have been conducted on the interaction of chemical pollutants and the epidemiology of infectious disease.

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Malaria has long been recognized by health officials in Brazil to be associated with gold mining activity, and control of malaria in mining regions is a high priority in Brazil¹⁰. In the States of Pará and Rondônia, where extensive gold mining activities are occurring, the prevalence of malaria and API rates are the highest in the country²⁵. In 1994, these two states accounted for over half of all reported cases of malaria in Brasil²⁵. Artisanal mining of alluvial gold creates ecologic changes (deforestation, destruction of aquatic systems, creation of pools in place of free flowing streams and rivers) that increase breeding niches for the *Anopheles* mosquito vectors of malaria. Mining also increases the size of dispersed settlements⁸ often of individuals from other parts of Brazil (where malaria is largely absent) to Amazônia, which results in exposure of immunologically naive persons to infection.

Gold mining within the Brazilian Amazon is conducted by some large scale operations but mostly by small scale miners, or *garimpeiros*, who extract gold from dredged river bed and bank sediments. Elemental mercury is used in an open process. First, the gold in sediments is amalgamated crudely by hand mixing of liquid elemental mercury with sediments forming a gold-mercury amalgam. Second, the amalgam is burned to remove the mercury. This refining process is usually begun at the *garimpo*, using propane heat sources, and then finished in "casas de ouro" in small towns where gold is bought and sold⁶. In both amalgamation and burning, the *garimpeiros* experience significant dermal and inhalation exposures to mercury^{5 15}. Substantial amounts of mercury are released into the environment from amalgamation and also in some regions from soil erosion^{17 33}. Increased mercury levels in fish and sediments in downstream ecosystems have been documented^{19 20 21}. Exact figures on gold production and

mercury use are unavailable since much of this activity is illegal and unreported. It is estimated by CETEM (Brazilian Council on Mining Technology) that about 14 metric tons of gold are mined in this fashion each year in the state of Pará (Villas Boas, 1999 personal communication). For every kilogram of gold mined by the *garimpeiros* through uncontrolled processes, at least one kilogram of mercury is released into the environment¹⁷. Despite attempts to introduce appropriate technology, few attempts at mercury recovery are made at any stage in the process.

This situation has stimulated us to investigate possible interactions between toxic chemical exposures and infectious diseases. Mercury is a well characterized immunotoxic metal and it is reported to impair host responses to viral infections in animal models^{13 18}. We have recently reported that mercury exposure of BALB/c mice impairs resistance to infection and blocks immunity to the murine plasmodium, *Plasmodium yoelii*²⁷, and Bagenstose et al² reported that mercury can also interact with leishmaniasis in mice.

The objectives of this study are to describe the extent of exposures to mercury and malaria in a group of miners (*garimpeiros*) and their helpers at a single gold mining site (*garimpo*) in the Tapajós River area in the State of Pará, Brazil, and to evaluate any evidence for interactions between mercury exposure and malaria infection. The specific hypothesis of interest is whether or not there is a positive association between mercury exposure, as determined by blood and urinary mercury levels, and malaria prevalence, as determined by parasitemia. The site selected for this initial investigation is a gold mining site in the Brazilian Amazon, where the miners are exposed both to mercury in amalgamation and crude refining, and to the local *Anopheles* vector of malaria.

MATERIALS AND METHODS

In 1997, a team of two physicians trained in tropical medicine (GTS and RSUS), four medical technicians, and a project co-coordinator flew to an airstrip at the Piranha *garimpo* in the State of Pará. This site is located in an inaccessible region of the Tapajós watershed approximately 200km south of Itaituba. Chosen for its use of mercury in the mining process as well as being an area of malaria endemicity (Jair, FNS-Itaituba, personal communication), the Piranha site is active year round and has been in operation since 1962. Selection of and access to the site was arranged in cooperation with the Associations of Mine Owners and Mine Workers of the Tapajós. Over a six day period, a total of 135 people working in the *garimpo* gave informed consent and agreed to participate in a cross sectional survey. This represented almost the entire *garimpo* population and included everyone except those from the most isolated sites or those who for other reasons could not get to the airstrip/trading post where the interviews and exams were conducted.

A medical history and physical exam were performed. Two 15-ml whole blood samples and a 20-ml urine specimen were collected from each subject for laboratory tests. Methods for blood collection are the same as used by Grandjean et al (1999)¹². The urine samples were prepared for mercury analysis in Rio de Janeiro and Santarém, Brazil. Blood and urinary mercury levels were measured by Atomic Absorption Spectroscopy in the laboratory of Dr. O. Malm, Universidade Federal do RJ, which participates in an international QA/QC program. Malaria infection was assessed by a Giemsa-stained thin blood film obtained from a finger prick. The slides were examined microscopically at the *garimpo* by a technician from the Itaituba office of the Fundação Nacional de Saúde (FUNASA) and then reexamined by a technician at the Evandro Chagas Institute in Belém (blinded to the initial assessment). A detailed questionnaire in Portuguese ascertained self-reported history of malaria and other infections, health history, and details of mercury use/

exposure, as well as demographic and lifestyle characteristics.

All statistical analyses were performed using SAS JMP software for Macintosh. ANOVA was used to assess statistical significance for continuous

variables and a chi square test was used for categorical variables. The study protocol was approved by the Institutional Review Boards at the University of Maryland Medical School, and by the Evandro Chagas Institute - FUNASA.

RESULTS

All subjects who came to the study site agreed to participate in the study. The majority of the participants were male (Table 1). The mean age was 33.1 and ranged from 2 to 58 years. Almost 90% had not completed primary level education. Over 70% were smokers and a

Table 1 - Selected demographic characteristics of a gold mining population from Pará, Brasil.

	N	%
Gender		
male	104	77.0
female	31	23.0
Age, mean (SD)	33.1	9.6
Education level,		
literate	28	20.7
primary grade incomplete	92	68.1
primary grade complete	8	5.9
> primary grade complete	7	5.2
Smoking		
current smoker	84	72.7
pack years, mean (SD)	8.4	9.0
Current alcohol use	93	72.7
Fish consumption		
< once per week	29	21.5
once per week	59	43.7
2-3 times per week	40	29.6
> 3 times per week	7	5.2

similar percentage reported alcohol use. Almost 80% consumed fish, a potential dietary source of mercury in this region²⁰. at least once per week. More than half of the subjects reported prior episodes of malaria infection (Table 2); while 18% reported having a prior episode of

Table 2 - Self-reported data on malaria, leishmaniasis, and tuberculosis among gold miners from Pará, Brasil.

Number of past malaria infections	N	%
Never	5	3.8
1x	23	17.3
2x	16	12.0
3x	10	7.5
4x	11	8.3
5+	68	51.1

cutaneous leishmaniasis infection and two individuals reported having had tuberculosis. The average age of entry into the mining occupation was 22.4 years. The occupation prior to mining for 40% was agriculture (Table 3). With respect to mercury use, the population fell into two groups: reporting either frequent use or none at all.

Table 3 - Distributions of factors related to mercury exposure among gold miners from Pará, Brasil.

Self-report	N	%
Frequency of mercury use		
frequently	74	59.2
rarely	7	5.6
never	44	32.6
Use mercury for		
amalgamation	65	86.7
other	10	13.3
Use of personal protective equipment		
nothing	77	91.7
mask	6	7.1
boots	1	1.2
Age began mining, mean (SD)	22.4	7.9
Occupation before mining		
agriculture	54	58.8
other	77	41.2
Laboratory tests, mean (SD)		
blood mercury (ug/dl)	25.6	16.3
urinary mercury (ug/dl)	21.5	20.5

Amalgamation was the most common use of mercury, while 13% reported using mercury for other purposes. The mean levels of mercury in the blood and urine were 25.6ug/dl and 21.5ug/dl, respectively (Table 3). Frequency distributions for each mercury biomarker are shown in Figure 1. The majority of these values were well in excess of the World Health Organization exposure limit guidance³⁵ for both blood (74% above) and urinary (52% above) levels of mercury. No one reported using appropriate personal protective equipment when handling mercury and no equipment was observed at the site (Table 3).

On examination (Table 4), 4 (3%) of the participants were febrile with temperature greater than 37.7°C. Four individuals were considered to be icteric by the examiners; 12 had edema, and 20 had skin ulcers which were not typical of cutaneous leishmaniasis. Eight individuals were hypertensive (blood pressures of systolic >140mmHg or diastolic >90 mm Hg). Giemsa-stained blood films were read for 133 subjects; 26 (19%) were positive: 14 for *Plasmodium vivax*, 11 for *P. falciparum*, and 1 for *P. malariae* (Table 4). This distribution of plasmodia is similar to that reported by PAHO²⁵.

Many individuals reported experiencing some symptoms (e.g., fatigue, headache, arthralgia, anorexia, memory loss, and insomnia) which might be related to

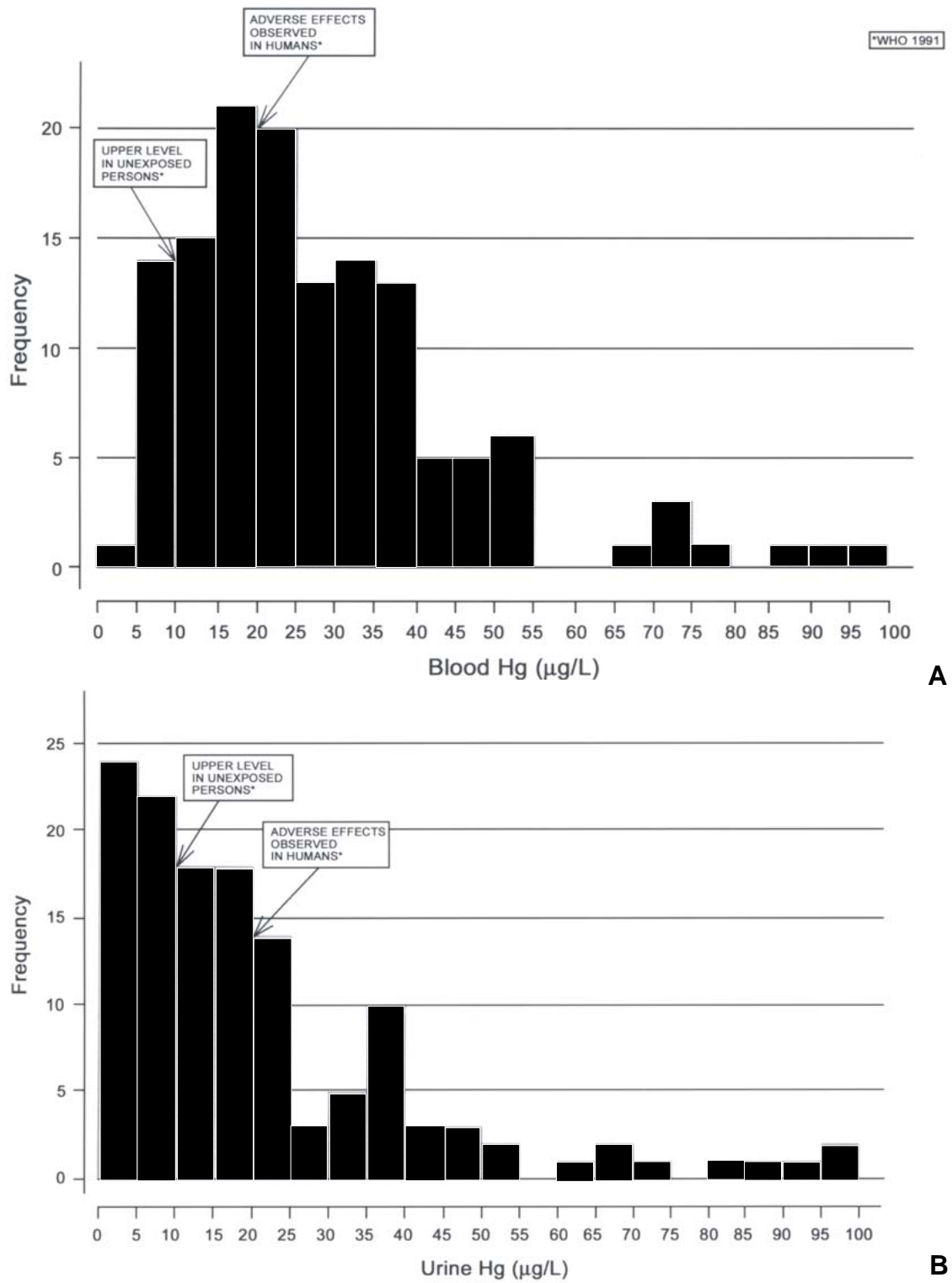


Figure 1 - Histogram of blood (a) and urinary (b) mercury levels among 135 persons associated with a Brazilian gold mine.

Table 4 - Selected clinical and laboratory findings among gold miners from Pará, Brasil.

	N	%
Clinical exam		
febrile (temp $\geq 37.7^{\circ}\text{C}$)	4	3.2
icteric,	4	3.2
edema	12	10.4
skin ulcers	20	15.9
Abnormal findings		
liver	25	15.9
spleen	35	27.6
lung	3	2.4
eye	2	1.6
abdomen	4	3.2
Laboratory tests		
positive for malaria	26	19.4
type of malaria		
malariae	1	3.8
vivax	14	53.9
falciparum	11	42.3

mercury exposure (Table 5). However, when comparisons were made in groups stratified by blood and urinary mercury levels, the results showed that no relationships between these symptoms and mercury exposure.

Levels of mercury in the blood and urine were not predictive of prevalent malaria infection (Table 6). Self-reported exposure to mercury was also not predictive of current malaria infection. Duration of employment at the *garimpo* and history of mining were both significantly, but inversely, associated with the relative odds of current malaria infection. Individuals who had been working at the *garimpo* for less than one year or had been employed in mining for less than 10 years were significantly more likely to be infected with malaria at the time of the examination (OR 3.1, 95% CI 1.0-9.0; OR 2.8, 95% CI 1.0-8.0, respectively). Gender was not associated with malaria prevalence. However, compared to individuals with no or only one prior episode of malaria, those with more prior episodes were more likely to be infected with the parasite (Figure 2).

Table 5 - Current clinical symptoms related to mercury exposure by blood and urinary mercury quartile among a gold mining population from Pará, Brasil.

	Total	Blood mercury					p (chi square)	Urinary mercury					p (chi square)
		Quartile 1	Quartile 2	Quartile 3	Quartile 4	Quartile 1		Quartile 2	Quartile 3	Quartile 4			
Skin ulcers	20 (14.8)	4 (11.8)	7 (20.6)	4 (11.8)	5 (15.2)	0,72	6 (17.7)	6 (17.7)	4 (11.8)	4 (12.1)	0,83		
Anorexia	37 (27.4)	8 (23.5)	7 (20.6)	13 (38.2)	9 (27.3)	0,39	9 (26.5)	8 (23.5)	9 (26.5)	11 (33.3)	0,84		
Fatigue	63 (46.7)	15 (44.1)	12 (35.3)	21 (61.8)	15 (45.5)	0,17	13 (38.2)	14 (41.2)	14 (41.2)	22 (66.7)	0,07		
Headache	48 (35.6)	17 (50.0)	9 (26.5)	11 (32.4)	11 (33.3)	0,21	14 (41.2)	11 (32.4)	12 (35.3)	11 (33.3)	0,88		
Myalgia	23 (17.0)	7 (20.6)	9 (26.5)	2 (5.9)	5 (15.2)	0,11	10 (29.4)	3 (8.8)	4 (11.8)	6 (18.2)	0,12		
Arthralgia	41 (30.4)	11 (32.4)	11 (32.4)	11 (32.4)	8 (24.2)	0,85	9 (26.5)	12 (35.3)	13 (38.2)	7 (21.2)	0,39		
Vision problems	28 (20.7)	9 (26.5)	5 (14.7)	6 (17.7)	8 (24.2)	0,59	7 (20.6)	9 (26.5)	7 (20.6)	5 (15.2)	0,73		
Insomnia	31 (23.0)	9 (26.5)	6 (17.7)	12 (35.3)	4 (12.1)	0,11	9 (26.5)	6 (17.7)	6 (17.7)	10 (30.3)	0,51		
Memory loss	33 (24.4)	13 (38.2)	6 (17.7)	6 (17.7)	8 (24.2)	0,17	8 (23.5)	9 (26.5)	6 (17.7)	10 (30.3)	0,66		
Tremors	25 (18.5)	6 (17.7)	4 (11.8)	10 (29.4)	5 (15.2)	0,29	8 (23.5)	11 (32.4)	4 (11.8)	2 (6.1)	0,02		

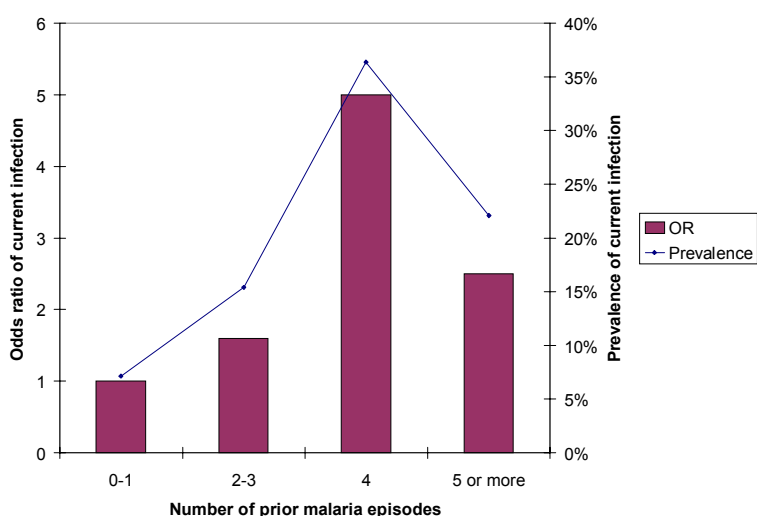


Figure 2 - Prevalence and odds ratio of current malaria infection by number of prior malaria episodes.

Table 6 - Odds ratio and 95% confidence interval for current malaria infection among persons associated with a gold mine in Pará, Brasil.

	OR (95% CI)
Quartile of blood mercury	
2 vs. 1	0.51 (0.16-1.6)
3 vs. 1	0.43 (0.13-1.4)
4 vs. 1	0.43 (0.13-1.4)
Quartile of urinary mercury	
2 vs. 1	1.21 (0.36-4.1)
3 vs. 1	1.04 (0.30-3.6)
4 vs. 1	1.26 (0.37-4.2)
Frequent mercury exposure vs. rare or never	1.01 (0.4-2.6)
Duration of employment <1 yr at this garimpo vs. ≥ 1 yr.	3.07 (1.0-9.0)*
Duration of employment in mining <10 years vs. ≤ 10 years	2.82 (0.99-8.0)*
Malaria history	
2-3 prior episodes vs. 0-1	1.58 (0.32-7.8)
2-4 prior episodes vs. 0-1	4.95 (0.89-27.5)
5+ prior episodes vs. 0-1	2.45 (0.65-9.2)
Sex (male vs. female)	1.29 (0.49-3.4)

* P<0.1

Three of 26 parasitemic individuals were febrile at examination and those with parasitemia were more likely to report a febrile episode within 3 weeks of the exam (30.8% vs. 17.6%). Parasitemic

individuals were more likely to have symptoms compatible with malaria infection, but the difference was only statistically significant for chills ($p=0.03$) (Table 7).

Table 7 - Table of malaria-related symptoms by parasitemia status.

	No parasitemia (n=109)	Parasitemia (n=26)	p
Temperature (C), mean	36.2	36.8	0,0007
Self-report (%)			
Fever	17.6	30.8	0,1483
Fatigue	46.3	50.0	0,8615
Chills	12.0	30.8	0,0276

DISCUSSION

This investigation of small scale gold mining in Brazil found high levels of mercury exposure. Although symptoms compatible with mercury toxicity were prevalent, these were nonspecific in nature and there was no statistical correlation was observed between levels of mercury exposure and reported or observed symptoms. These data are consistent with reports by others on occupational exposures to mercury in artisanal gold mining in Amazônia. Branches et al (1993)⁵ reported somewhat lower exposures among goldmines in Pará in 1993; a similar range of nonspecific symptoms were also reported in these subjects, as well as signs of neurological dysfunction by clinical examination. We are unaware of any cases of clinical mercury poisoning having been reported in the published literature in gold miners in Pará to date. The levels found in most of the subjects in our study are well above health guidelines from WHO³⁵. Compared to levels of mercury in blood for North American populations without occupational exposure,

all persons had 10-100 fold elevations in blood mercury²³. These garimpeiros also had significantly higher levels of urine and blood mercury as compared to most of the Amazonian populations exposed only to mercury via fish consumption (methyl mercury)^{20 21}. These data confirm that occupational exposures in artisanal gold mining and crude refining are of the greatest immediate health concern^{5 6 9 16}.

Malaria has re-emerged as a major problem in South America during the last decade. During 1988, in Loreto, Peru, part of the greater Amazon region, there were no reported cases of malaria. In 1991, there were 140 cases, followed by an explosive annual increase in the number of cases, such that in 1997 there were 121,268 reported cases, including 54,290 slide confirmed cases of *P. falciparum*¹⁴. In Brazil, the overwhelming majority of reported malaria cases occur in the gold mining areas of the Amazon region. Gold mining contributes to rates and spread of malaria through the ecologic changes associated with mining

operations for several reasons: 1) gold mining activities bring persons who are immunologically naive to malaria into direct contact with the mosquito vector and the infectious agent; 2) mining methods create ecological niches for mosquitoes to breed, propagate, and survive in pools of water; 3) mining operations ensure many repeated contacts between the human reservoirs and the mosquito vector; 4) mining settlements in remote areas are often inaccessible to periodic health surveillance, diagnosis and treatment; and 5) the sociological context of gold mining involves continual out-migration of infected persons, creating a mobile reservoir of human hosts to transfer disease locally and distantly, both in and outside of Brasil^{26, 29}.

This latter factor may explain the association between gold mining and malaria cases outside the Amazon region. A tracing study by de Souza et al (unpublished) demonstrated that over 1,000 cases

occurring as far away as Rio de Janeiro could be linked to contacts with a gold mining site in the Tapajós region of Pará (Figure 3). The episodic nature of gold mining as an occupation⁸ and the movement of persons in and out of gold mining regions in Brazil contribute to this dispersion.

Mercury exposure among the miners may also play a role in malaria transmission in Brazil. Mercury is known to affect the immune system. Mercury induced autoimmunity is associated with nephropathy in rodents and humans^{11, 13}. Recent studies in which mice were exposed to non-lethal doses of malaria showed an attenuated Th1 immune response, ultimately resulting in decreased release of macrophage and splenocyte nitric oxide^{27, 28}, which is specifically instrumental in a normal immune response to malaria and acquisition of immunity in a murine model^{31, 32}. We have also found that low doses of mercury increase



Figure 3 - Trace back diagram of malaria cases occurring in 1992 outside of Amazonia, data from da Souza JM. The shaded area in the State of Pará (PA) indicates the region in which all traced cases were found to have contacted plasmodia; this is the region of intensive gold mining of the Tapajós watershed. Abbreviations for states of Brazil: PA – Pará; MT – Mato Grosso; GO – Goiás; MA – Maranhão; CE – Ceará; MS – Mato Grosso do Sul; MG - Minas Gerais; BA – Bahia; RJ – Rio de Janeiro; ES – Espírito Santo; SP – São Paulo; PR – Parana; PI – Piauí; RN – Rio Grande do Norte; PB – Paraíba; PE – Pernambuco; AL – Alagoas; SE – Sergipe; AP – Amapá; RR – Roraima; AM – Amazonas; RO – Rondonia; AC – Acre; SC – Santa Catarina; RS - Rio Grande do Sul (Note: Tocantins is not shown).

host susceptibility to challenges of direct malaria infection and block the acquisition of immunity to *P. yoelii* in the irradiated sporozoite model²⁷. Bagenstose et al (2002) recently reported that mercury can also interact with leishmaniasis in an animal model².

We did not find a direct association between mercury exposure and malaria prevalence in our sample, possibly due to the timing of our study, during which a relatively small number of prevalent cases found in this cross sectional study. The current investigation has generated some support for hypotheses regarding a possible effect of mercury on the acquisition of immunity to malaria. Individuals in this garimpo who reported a history of 4 or more prior episodes of malaria infection were more likely to have prevalent malaria infection as compared to those with a self-reported history of 3 or fewer malaria episodes (Figure 2). This pattern is not consistent with experience that suggests that past history of malaria infection reduces the odds of prevalent malaria. For example, in hyperendemic areas, acquisition of immunity to malaria was reported to occur after 3 or more infections with the parasite³. Our observations are consistent with the hypothesis that mercury exposure may interfere with the expected natural acquisition of immunity to malaria, as found in our murine model²⁷. However, confirmation of this hypothesis will require a prospective study of malaria transmission, infection, and mercury exposure.

The relationship between ecologic/environmental change and infectious disease has received increasing worldwide attention³⁴. A memorable example of the effect of development is the building of the Aswan High Dam in Egypt, which was followed by an increase in the distribution of the vector and the size of the exposed population exposed to schistosomiasis³⁰. However, virtually no attention has focused on the ecologic and environmental impacts on infectious disease of *chemical contamination*, which accompanies industrialization and resource exploitation in many developing countries.

Our study was limited in several respects. We only assessed exposures to inorganic mercury, associated with gold mining. Some subjects may have also been

exposed to methyl mercury from consuming mercury-contaminated fish. Our measurements of mercury were in blood and urine, rather than hair, and were of total mercury only. We may not have found the garimpeiros most severely affected by mercury in Piranha, since those individuals may not have been able to walk to the site of our field clinic. At the garimpo many of the workers were living at *baixãos* (or lower areas), up to 8 hours away on foot. The small size of the sample, with only 26 persons having current parasitemia, prevented us from rigorously testing associations in subgroups, such as those who had been at the *garimpo* for varying periods of time. Self-report data on prior malaria infections may have been unreliable, representing only history of fever (no parasitological confirmation was available at the garimpo), or recurrent febrile episodes of the same primary malaria infection, which could have been inadequately treated. Finally, because of the cross-sectional design, we could not directly test the hypothesis that mercury exposures subsequently alter human resistance to malaria.

Our investigation documents and underscores the concern that widespread use and significant exposures to mercury occur in Brazilian *garimpos*, despite policies prohibiting its use in gold amalgamation. Previous studies have reported similar findings on smaller groups^{5,7,9}. There is an urgent need to control exposures to mercury among the *garimpeiros*, in order to prevent mercury intoxications, regardless of any interactions with malaria susceptibility. Since mercury use is already illegal in Brazil, policy recommendations alone are not effective. If mercury exposure turns out to be linked to a proportion of Brazil's malaria problem, a paradigm shift in the policy debate on mercury use may gain some momentum. Thus, while our investigation was not able to test the mercury-immunity hypothesis directly, we believe there is sufficient evidence and need to pursue further field investigations with regard to mercury exposure and acquisition of immunity to malaria in Brazil and other countries with artisanal use of mercury in mining. The prevention and treatment approaches currently applied to the *garimpos* are inadequate and must be increased.

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