Methylmercury Neurotoxicity in Amazonian Children Downstream from Gold Mining

Philippe Grandjean,[1,2] Roberta F. White,[1,2] Anne Nielsen,[1] David Cleary,[3] and Elisabeth C. de Oliveira Santos[4]

[1]Department of Environmental Medicine, Odense University, Odense, Denmark; [2]Departments of Environmental Health and Neurology, Boston University Schools of Medicine and Public Health, Boston, Massachusetts, USA; [3]IC Consultants Ltd., Imperial College, London, United Kingdom; [4]Instituto Evandro Chagas, Universidad Federal do Pará, Belém, Brazil

In widespread informal gold mining in the Amazon Basin, mercury is used to capture the gold particles as amalgam. Releases of mercury to the environment have resulted in the contamination of freshwater fish with methylmercury. In four comparable Amazonian communities, we examined 351 of 420 eligible children between 7 and 12 years of age. In three Tapajós villages with the highest exposures, more than 80% of 246 children had hair-mercury concentrations above 10 µg/g, a limit above which adverse effects on brain development are likely to occur. Neuropsychological tests of motor function, attention, and visuospatial performance showed decrements associated with the hair-mercury concentrations. Especially on the Santa Ana form board and the Stanford-Binet copying tests, similar associations were also apparent in the 105 children from the village with the lowest exposures, where all but two children had hair-mercury concentrations below 10 µg/g. Although average exposure levels may not have changed during recent years, prenatal exposure levels are unknown, and exact dose relationships cannot be generated from this cross-sectional study. However, the current mercury pollution seems sufficiently severe to cause adverse effects on brain development. *Key words*: environmental pollution, exposure assessment, food contamination, hair analysis, mercury poisoning, neuropsychological tests, prenatal exposure delayed effects. *Environ Health Perspect* 107:587–591 (1999). [Online 14 June 1999]
http://ehpnet1.niehs.nih.gov/docs/1999/107p587-591grandjean/abstract.html

Amalgamation with elemental mercury has been used for gold production since antiquity (*1,2*). Dredged sediments or soil are washed through sluice boxes, and the mercury then captures the alluvial or colluvial gold particles. A dramatic rise in gold prices in 1979 spurred a major gold rush in the Amazon region (*1*) that continues, albeit on a reduced scale, to the present day. Reliable data on mercury consumption in the informal sector gold mining processes do not exist. However, from production statistics, the annual mercury losses in the Brazilian Amazon during recent years are thought to have exceeded 100 tons (*1–3*). Following methylation in the environment, methylmercury contaminates freshwater biota, and substantial mercury accumulation in piscivorous fish has been found downstream from gold-mining areas in the Amazon Basin, with concentrations often exceeding 0.5 µg/g (*2,4–6*). However, detailed exposure assessment is difficult because of the large number of different species consumed.

Exposure of riverine populations to increased amounts of methylmercury from their fish diet has been documented by increased hair-mercury concentrations in frequent fish consumers (*5–8*). Thus, the health hazards caused by methylmercury contamination are of serious concern in communities that depend on fish as a staple diet. Methylmercury toxicity is particularly harmful to the developing brain (*9,10*), and exposures are therefore most hazardous during pregnancy. Cognitive deficits have recently been reported in 7-year-old children with known prenatal exposures to this neurotoxicant (*11*). However, similar prospective studies of birth cohorts would be very difficult to carry out in Amazonian riverine communities. Epidemiologic designs of a more limited time scale seem to be indicated.

We carried out cross-sectional studies in four comparable riverine communities in the Brazilian Amazon Basin. Children 7–12 years of age were examined, as neurobehavioral tests are most informative in children who have reached school age. Also, this age group would have had a lifelong exposure to methylmercury, including prenatal exposure from the mother's fish diet. In these riverine communities, current exposure levels are likely to reflect past dietary habits as well.

Materials and Methods

The Tapajós river was selected for this study because the headwaters house the largest and oldest informal sector gold field (Figure 1) (*1*). In this Amazonian river system, long-term mercury contamination would be expected to have most severely affected the local population. Deforestation, automobile traffic, and industrialization are limited, especially upstream from Villages C (Sao Luis do Tapajós) and D (Sai-Cinza), and exposure to environmental neurotoxicants other than mercury is therefore unlikely. Village B (Brasilia Legal) was thought to be less exposed, as the contaminated water became diluted further downstream. A village just beyond the junction of the Amazon and Tapajós rivers was selected for comparison (Santana do Ituquí; Figure 1). Each riverine community selected had approximately 500 inhabitants and a primary school with compulsory attendance up to 12 years of age. A household survey was carried out beforehand to obtain demographic data and to disseminate the invitation for health examinations.

The field team included nurses and medical doctors with many years of experience performing field studies in the Amazon. They were responsible for the interviews, physical examinations, and tropical disease tests. A medical student administered the motor-function tests, and the other neuropsychological tests were administered by a nurse; both had been specially trained to conduct the tests in a uniform fashion. All examinations were carried out without any knowledge concerning mercury exposures. Interviews and medical data were coded in Belém, Brazil, and neuropsychological tests were scored in Odense, Denmark, and Boston, Massachusetts.

Of the 420 children 7–12 years of age recorded as residents of the four communities, 351 (84%) were examined. A medical team from the Federal University of Para (Belém) offered comprehensive health examinations to the children and to women of child-bearing age (younger than 45 years of age). Thus, the 135 mothers of 252 of the children were examined, and hair samples for mercury analysis were obtained from the 114 mothers of 222 children examined. No refusals were recorded, and absence from the examinations appeared to be due to temporary work at farm plots, fishing trips, visits to other settlements, or occasional cases of disease.

Address correspondence to P. Grandjean, Institute of Public Health, Winslowparken 17, 5000 Odense, Denmark. Telephone: 45 65 57 37 69. Fax: 45 65 91 14 58. E-mail: p.grandjean@winsloew.ou.dk

This study was supported by the DG-1 Tropical Forest Programme (B7-6201) of the European Commission, by Imperial College Consultants, London, and by the Danish Medical Research Council.

Received 9 November 1998; accepted 22 March 1999.

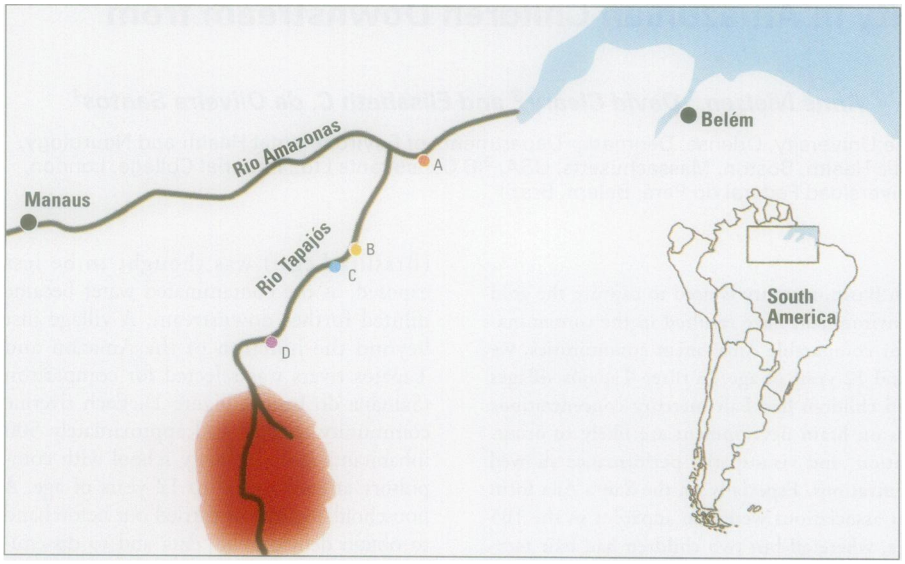

Figure 1. Southeastern part of the Amazon Basin, showing the location of the study sites. Three villages [B, Brasilia Legal; C, Sao Luis do Tapajós; and D, Sai-Cinza] were located on the Rio Tapajós, a major tributary to the Rio Amazonas. Almost all gold mining in this region takes place on the upper Tapajós (shaded area). Village A, Santana do Ituquí, was located near the junction of the two rivers.

Interviews of the mothers confirmed that social circumstances within and between the communities varied little. Thus, illiteracy was common, and 48.4% of the mothers had not received education beyond primary school. Only seven women (5.3%) had attended secondary education outside the community. Paternal employment was almost exclusively in subsistence farming and in subsistence and commercial fishing. Because of tradition and poverty, 78% of the mothers were alcohol abstainers, and only four women (3%) regularly had alcohol up to once per week. Although the questionnaire did not attempt to elucidate circumstances at the time of the pregnancies, the living conditions appeared to have changed little during the previous several years. Information was also obtained on the past medical history of each child. In the absence of birth certification, the age of each child (in years) was given by the mother; in Village D, the age was verified from the records of the local health service.

For assessment of mercury exposure (*12*), we used the mercury concentration in a hair sample cut close to the scalp in the occipital region. Two centimeters of hair closest to the root were used for analysis. The hair sample was dissolved in nitric acid in a CEM microwave oven model MDS-2000 (CEM Corp., Indian Trail, NC), and the mercury content was determined by atomic absorption spectrometry on a Perkin-Elmer Flow Injection Mercury System model FIMS 400 with an AS-90 autosampler (Perkin-Elmer, Norwalk, CT), as previously described (*11,13*). These analyses were performed at the laboratory established as part of the project at Fundaçao Esperança, Santarem, Brazil. Analyses were performed in cooperation with similar laboratories at the Federal University in Rio de Janeiro, Brazil, and at Odense University, Denmark; analyses of split hair samples confirmed a high analytical quality, with an average coefficient of variation of 14.3% over the full exposure interval.

Based on overall criteria for neuropsychological test selection (*14*) as also applied in a previous study (*11*), feasible and appropriate neurobehavioral tests were chosen to evaluate possible subtle signs of methylmercury neurotoxicity in the children. Further, we considered the practical circumstances of the field study, differences in language and culture, and time constraints. The tests chosen mainly reflect motor function, attention, visuospatial function, and short-term memory, which are sensitive targets of methylmercury neurotoxicity (*11,14*).

For the finger-tapping task (*15*), the child tapped a key for 15 sec first with the preferred hand for practice, then twice with the preferred hand, and twice with the nonpreferred hand. We used the standard board for adults (Psychological Assessment Resources, Odessa, FL), but shortened the tapping arm so that it was appropriate for the hand sizes of the children. Scores consisted of the maximum number of taps in each condition. This task is a measure of manual motor ability that focuses specifically on speed.

The Santa Ana form board has four rows of square holes into which square pegs with a cylindrical head will fit (*15*). We produced the board and pegs by computer-aided technology to ensure that all pegs and holes were the same sizes. Half of the circular area on the top of each peg is white and the other half is black. The subject had to lift each peg and rotate it 180°. The score was the number turned in 60 sec with the dominant hand, the nondominant hand, and both hands. This test measures motor coordination and dexterity.

On the Wechsler Intelligence Scale for Children-III Digit Spans Test forward condition (*16*), digit spans of increasing length were presented until the child failed both trials in a series of the same length. Score was total number of correct trials. This test evaluates attention and information processing.

Two subtests from the Stanford-Binet Intelligence Scale (*17*) were used. On the copying test, the child copied visual designs through the use of geometric forms and by drawing. A memory condition was added where the number of designs remembered after 20 min was recorded. This test assesses visuospatial and visuoconstructional function. The bead memory test is a nonverbal memory task in which the child replicated designs made of beads.

Tests were given in Portuguese by the same examiner in each village, although in village D an interpreter was used for administration of tests feasible in Mundurucú. Although all tests were carried out in community A, parts of the test battery were left out in villages B–D for logistic reasons. The study protocol was developed in accordance with the Brazilian Ministry of Health guidelines to satisfy the requirements of the Helsinki convention. Informed consent was obtained from the mothers.

The relation between mercury exposure and neurobehavioral function was analyzed by multiple regression analyses with adjustment for relevant covariates. In addition to age and sex as obligatory variables, health status, maternal education, and maternal marital status were examined as independent variables because these factors seemed to vary the most and would be expected to affect neurobehavioral development. To adjust for possible community-based differences, dummy variables for residence were explored.

Results

Hair-mercury concentrations approached log normal distributions with overall geometric means of 11.0 µg/g (median, 12.8 µg/g) and 11.6 µg/g (median, 14.0 µg/g) for children and their mothers, respectively. These averages exceed an estimated limit of approximately 10 µg/g, above which a discernible risk of developmental neurotoxicity is thought to occur (*9,10*). As expected, the mercury exposures differed between the communities, with the lowest results occurring in village A beyond the junction with the Amazon River, where only 2 of 105 children had a hair-mercury concentration above 10 µg/g. On the Tapajós villages B, C, and D, 58 of 76, 65 of 71, and 80 of 87 children, respectively, exceeded this limit (Figure 2).

Maternal hair-mercury concentrations were highly correlated with those of their children (r = 0.80 after logarithmic transformation). This result was expected, as most meals are shared within each household. A maternal hair sample was unavailable for 129 (37%) of the children; therefore, the child's current hair-mercury concentration was used as the exposure biomarker in all data analyses. In Village B, boys and girls had similar hair-mercury concentrations, but boys in the other villages averaged approximately 20% higher hair concentrations than the girls. The mercury concentrations were not associated with the age of the child.

Dietary habits were similar in the four settlements, with most children eating fish at two meals every day. In Village A, 80 children said to be eating fish twice every day had a higher hair-mercury concentration than the 20 who had fish less often (geometric means 4.07 and 3.00 µg/g, respectively; p = 0.01). Likewise, in Village D, closest to the contamination source, 33 children who ate fish twice every day had higher hair concentrations than the 21 children who ate fish less often (19.99 and 15.79 µg/g, respectively; p = 0.04). In villages B and C, too few children ate fish less than twice per week to evaluate this association. The limited differences in dietary habits are also reflected in the narrow frequency distribution of the mercury concentrations within each community (Figure 2). Thus, methylmercury exposures in villages A and B barely overlapped with those in villages C and D. The exposure differences that did occur within individual villages were probably related to variations in access to fish, preferred fish species, portion sizes, and availability of agricultural products, but limited information collected in this regard did not allow any detailed consideration.

Upon physical examination of the children, no nervous system disease of other origin was identified. Blood samples showed no evidence of malaria. Fecal samples revealed prevalent intestinal diseases, mainly amebiasis, giardiasis, or infestation with roundworm (*Ascaris lumbricoides*) or hookworm (*Ancylostoma* sp.). In general, the children appeared fully capable of participating in the examinations, and none of the children had symptoms that appeared to influence their neurobehavioral performance. Also, the mercury exposure of children with some type of infectious disease did not differ from the one of other children in the community. Four children in the Tapajós communities had a hemoglobin concentration slightly below 110 g/L (6.8 mmol/L), indicating anemia, but hematology parameters were not associated with the mercury exposure level.

All neurobehavioral tests were successfully administered in Village A, and the tests used in the other villages also appeared to be fully feasible (Table 1). The distributions were approximately Gaussian. Unfortunately, published test results for Amazonian populations were not available. However, when compared to data from North American and European children of similar ages (*11,15–17*), overall averages for the Brazilian children were close to expectation for finger tapping, less on Digit Spans, and considerably lower on the Stanford-Binet tests. Comparison data were not available for the Santa Ana test.

Multiple regression analyses were carried out for Village A and for the total groups examined. After adjustment for age and sex, dummy variables for maternal education levels and maternal marital status barely changed the regression coefficients for the mercury exposure. The same applied to health status indicators. These covariates were therefore not included in the final equations. Although community was an important predictor in most analyses, adjustment for this variable may not be appropriate because of the widely different mercury exposures (Figure 2). Regression analyses of the total material were therefore carried out both with and without community adjustment (Table 2).

The Santa Ana form board and the Stanford-Binet copying test showed the

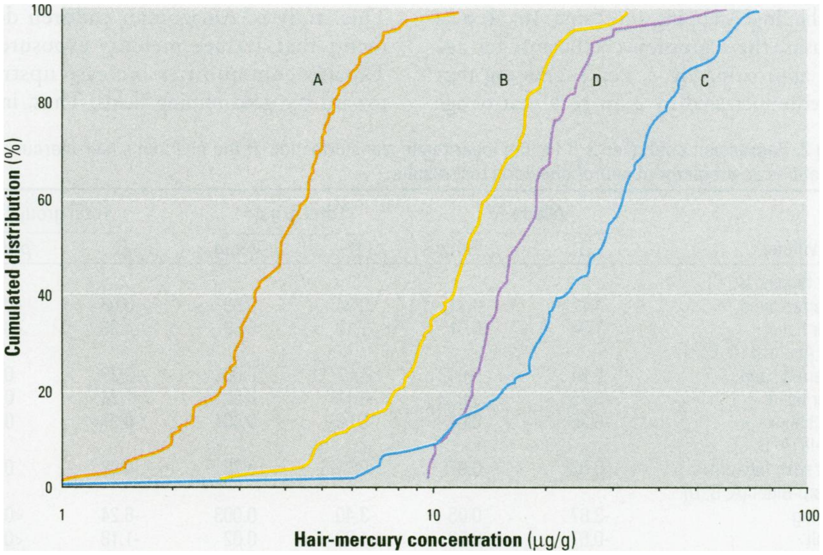

Figure 2. Cumulated distributions of hair-mercury concentrations in children from four riverine communities in the Brazilian Amazon. Abbreviations: A, Santana do Ituquí; B, Brasilia Legal; C, Sao Luis do Tapajós; D, Sai-Cinza.

Table 1. Children examined in villages A–D, their hair-mercury concentrations (geometric mean and range), and results of neurobehavioral tests (mean ± standard deviation).

	Village			
Parameter	A	B	C	D
Eligible children (no.)	124	112	98	86
Boys/girls examined (no.)	54/51	39/52	38/49	28/43
Age	9.50 ± 1.75	9.52 ± 1.68	8.98 ± 1.67	9.76 ± 1.79
Hair-mercury (µg/g)	3.80 (0.5–12.4)	11.9 (0.7–35.8)	25.4 (0.6–83.5)	17.7 (7.3–63.8)
Finger-tapping speed				
Preferred hand	54.7 ± 9.7	–	45.8 ± 8.4	–
Other hand	49.7 ± 8.9	–	43.6 ± 8.0	–
Santa Ana dexterity test				
Preferred hand	30.0 ± 6.0	–	28.0 ± 5.8	–
Other hand	28.0 ± 4.9	–	27.0 ± 5.4	–
Both hands	25.6 ± 6.8	–	24.9 ± 8.5	–
WISC-III				
Digit Span forward	6.60 ± 1.79	6.74 ± 1.86	5.92 ± 1.93	3.77 ± 1.51
Stanford-Binet Test				
Copying	18.1 ± 4.7	17.4 ± 4.9	–	10.6 ± 4.8
Recall	2.77 ± 2.37	2.63 ± 1.81	–	1.84 ± 1.59
Bead memory	14.2 ± 4.5	14.7 ± 4.2	–	10.1 ± 4.8

Abbreviations: A, Santana do Ituquí; B, Brasilia Legal; C, Sao Luis do Tapajós; D, Sai-Cinza; WISC, Wechsler Intelligence Scale for Children.

clearest associations with the hair-mercury concentration (Table 2). When the community parameter was left out of the regression equations, the mercury coefficients for the finger-tapping task increased considerably (Table 2, Figure 3). The opposite tendency was seen with the Santa Ana test. Overall, the regression coefficients for Village A seemed similar to those for the total group. When the Mundurucú community (Village D) was left out of the regression analyses for the Stanford-Binet results, mercury remained a significant predictor for the copying score (regression coefficient, -1.78; $p = 0.04$ after adjustment for community).

The regression coefficients for mercury (Table 2) may be compared to the ones for age, all of which were highly significant and which varied only little between the villages. For the finger-tapping and Santa Ana dexterity tasks, the regression coefficients for age were approximately 2, i.e., suggesting that the score increased by 2 for each year of age within the age interval studied. The regression coefficient for Digit Spans was 0.3, and for the three Stanford-Binet tasks, 1.6, 0.5, and 1.4, respectively. If the regression coefficient for the logarithmic transformation of the mercury concentration is of the same magnitude and in the opposite direction, that would mean that an increase in mercury exposure by a factor of 10 corresponds to a developmental delay of approximately 1 year.

Because the children were of different ages, an age times mercury interaction parameter was introduced in the regression analyses. The effect of mercury was significantly greater in younger children only for the nonpreferred hand condition of the Santa Ana test.

Discussion

This study of Amazonian children documents that average mercury exposures in Tapajós communities increase upstream toward the gold-mining fields. Thus, in the two villages furthest upstream, only a few children had hair-mercury concentrations below a limit of 10 µg/g (Figure 2). Most riverine children eat fish every day, usually twice each day. With the documented contamination of many fish species caught in the Tapajós, especially upstream (*2,4–6*), these results are not surprising.

Table 2. Regression coefficients β for the logarithmic transformation of the children's hair-mercury concentrations as predictor of neurobehavioral test results.

	Village A^a		Total group^b		Total group^a	
Test (village)	β	*p*-Value	β	*p*-Value	β	*p*-Value
Finger tapping (A, C)						
Preferred hand	4.12	0.31	0.04	0.99	-6.53	<0.001
Other hand	-1.84	0.61	-1.12	0.60	-4.36	<0.001
Santa Ana test (A, C)						
Preferred hand	-5.24	0.04	-4.57	0.002	-2.23	0.005
Other hand	-5.75	0.003	-4.12	0.001	-1.24	0.05
Both hands	-5.26	0.04	-5.58	0.001	-0.97	0.30
WISC-III (A, B, C)						
Digit span forward	0.03	0.97	0.11	0.79	-0.88	0.001
Stanford-Binet (A, B, D)						
Copying	-3.87	0.05	-3.40	0.003	-6.24	<0.001
Recall	-0.67	0.52	-1.23	0.02	-1.18	<0.001
Bead Memory	-0.56	0.74	-0.54	0.61	-2.91	<0.001

Abbreviations: A, Santana do Ituquí; B, Brasilia Legal; C, Sao Luis do Tapajós; D, Sai-Cinza; WISC, Wechsler Intelligence Scale for Children.

^{a}Adjusted for age and sex only. ^{b}Adjusted for age, sex, and community.

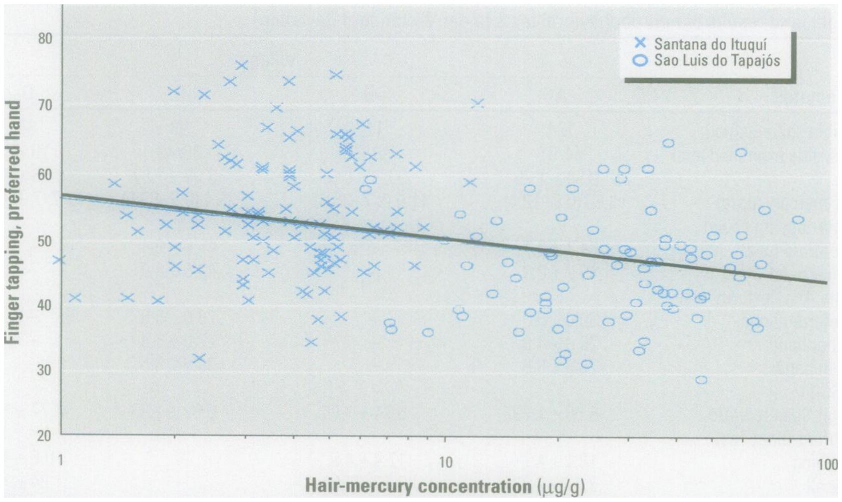

Figure 3. Finger-tapping results for the preferred hand obtained for 185 children 7–12 years of age from communities A (Santana do Ituquí) and C (Sao Luis do Tapajós). Their hair-mercury concentrations were not associated with age or sex; therefore, the unadjusted regression line is shown.

Although the mercury exposures are clearly in the range where neurotoxic effects may occur (*9–11*), the question is if these exposures are causing neurobehavioral decrements discernible in the Amazonian setting. The present study applied neurobehavioral tests thought to be culturally appropriate for children who had reached school age (*14*). Testing experience confirmed that the tests were feasible for the age group examined. However, test results may have been affected by current tropical diseases or past nutritional deficiencies. In a cross-sectional study in the Amazonian setting, adjustment for such factors would be difficult, but any imprecision for this reason would likely bias the overall results toward the null hypothesis of no effect of mercury exposure.

The design of the study allowed examination of four villages of the same size, where fish was the staple diet. Although three of the riverine communities were remarkably similar except for their location and mercury exposure, village D was a Mundurucú community that differed culturally from the others, and neuropsychological testing was conducted through an interpreter. Possible differences between the villages may involve school education, nutrition, or the relative extent of mercury exposure in the past. Whereas examination of more than 100 children from village A allowed separate analysis of this community, joint analyses of all villages showed results that were dependent on adjustment for community (Table 2). Because of the limited overlap in mercury exposure between the villages (Figure 2), such adjustment may not be appropriate. In this light, the regression coefficients for Village A alone may be most relevant, in particular the results for the Santa Ana form board and the Stanford-Binet copying test, which are in agreement with the overall relationship for all children examined.

As in a previous study (*11*), the use of a logarithmic transformation of the exposure variable was justified by the distribution of the hair-mercury results, and the transformed predictor provided a better fit with the outcome parameters than did a linear exposure parameter in the regression analyses. In neurobehavioral effect studies, a linear regression may be inappropriate, as a steep decrease at low exposure levels would predict outcome results below 0 at higher exposures. Although the exact shape of each dose–effect curve is unknown for the behavioral outcome measures, the size of this study does not allow any detailed evaluation in this regard. It is therefore possible that the use of logarithmic transformation of the exposure scale may have resulted in an underestimation of the dose relationship of the mercury effect.

The results (Table 2) may be compared to a recent study of almost 1,000 7-year-old Faroese children, where performance on neuropsychological tests revealed deficits in several functional domains at increased prenatal exposures to methylmercury (*11*). Thus, on a 15-sec computer-assisted finger-tapping task, the regression coefficients for the logarithmic transformation of the mercury concentration were approximately -2, i.e., intermediate between the results obtained here with and without adjustment for community. On the Digit Span Test, a small regression coefficient of -0.3 was recorded (*11*). In the present study, an effect of this magnitude would be difficult to detect because most of the children achieved scores of 5, 6, 7, or 8, thus limiting the statistical sensitivity of the test.

Effects on visuospatial performance were also seen in the Faroes (*11*), a finding that is in agreement with the association observed on the copying test in the present study. The bead memory test may have been too culturally challenging a task. Also, a recent study of mercury-exposed children from Madeira suggests that this test may not be sufficiently sensitive to detect subtle deficits caused by methylmercury exposure (*18*).

The Seychelles Child Development Study also measured maternal hair-mercury concentrations, but they were unrelated to neurodevelopmental results up to 5.5 years of age (*19*). However, despite the size of this prospective study, several sources of uncertainty limit its usefulness (*20*), and the tests used cannot be directly compared to the present study.

Although an association between mercury exposure and neurobehavioral deficit may be causal, the current mercury concentration in hair may not necessarily reflect the level of exposure that caused the adverse effect. Seasonal changes occur in river levels and in diet (*1,21*), but all communities were examined during the dry season. Also, the 3- to 4-cm hair samples analyzed would reflect the average mercury exposure during the past several months. Further, a biologic half-life of 6–8 weeks for methylmercury in the body (*22*) would tend to reduce the influence of short-term variations in intake on the exposure biomarker. However, longer term changes may have occurred, although studies of mercury concentrations in long strands of hair have shown no definite Amazon Basin trends during the 1990s (*3,23*). Still, any changes since the pregnancies in the late 1980s may not have affected the four villages and individual residents similarly. However, the fact that adjustment for community was included in the regression analyses and that significant associations were documented within Village A, which was thought to have been affected the least by the pollution, would support the validity of the associations.

In populations where diets change little over time, the current hair-mercury concentration of the mother has been used as a proxy indicator of the mercury exposure during pregnancy, i.e., the prenatal exposure of the child (*18*). In the Amazonian setting, where meals are usually shared within each household, hair-mercury concentrations in mothers and their children correlated highly. If no major dietary changes had occurred within the household, the current hair-mercury concentrations in both mother and child would also reflect past exposures, including the child's prenatal exposure level. Thus, given the close association between current maternal and child exposure levels, it is not possible in this study to separate the effects of prenatal and postnatal exposures.

It is not known whether mercury neurotoxicity is reversible, although patient reports on Minamata disease suggest that little improvement occurs after cessation of exposure (*9,10*). Within the span from 7 to 12 years of age, the children examined seemed to be affected by mercury to a similar degree, with the possible exception of one of the Santa Ana tasks. Older children may have had the opportunity to catch up in neurological development, whereas age-related test difficulty or differences in prenatal exposure levels could also have played a role. As a cross-sectional study, the evidence obtained cannot elucidate this issue.

The findings in this study suggest that these riverine children may not function as well intellectually as they would have in the absence of mercury exposure. This adverse effect may result in increased difficulties achieving the level of education and economic success that would otherwise have been possible. In such Amazonian communities, living circumstances vary little, as the inhabitants are united in poverty. This study suggests that many of them also share a hazardous mercury exposure and that mercury neurotoxicity may provide yet another obstacle in attempts to improve the quality of their lives.

REFERENCES AND NOTES

1. Cleary D. Anatomy of the Amazon Gold Rush. London:Macmillan, 1990.
2. Malm O. Gold mining as a source of mercury exposure in the Brazilian Amazon. Environ Res 77:73–78 (1998).
3. Akagi H, Malm O, Kinjo Y, Harada H, Branches FJP, Pfeiffer WC, Kato H. Methylmercury pollution in the Amazon, Brazil. Sci Total Environ 175:85–95 (1995).
4. Malm O, Branches JFP, Akagi H, Castro MB, Pfeiffer WC, Harada M, Bastos WR, Kato H. Mercury and methylmercury in fish and human hair from the Tapajós river basin, Brazil. Sci Total Environ 175:141–150 (1995).
5. Malm O, Guimaraes JRD, Castro MB, Bastos WR, Viana JP, Branches FJP, Silveira EG, Pfeiffer WC. Follow-up of mercury levels in fish, human hair and urine in the Madeira and Tapajós basins, Amazon, Brazil. Water Air Soil Pollut 97:45–51 (1997).
6. Bidone ED, Castilhos ZC, Cid de Souza TM, Lacerda LD. Fish contamination and human exposure to mercury in the Tapajós River basin, Pará State, Amazon, Brazil: a screening approach. Bull Environ Contam Toxicol 59:194–201 (1997).
7. Grandjean P, Cardoso B, Guimaraes G. Mercury poisoning [letter]. Lancet 342:991 (1993).
8. Cleary D, Thornton I, Brown N, Kazantzis G, Delves T, Worthington S. Mercury in Brazil. Nature 369:613–614 (1994).
9. International Programme on Chemical Safety. Methylmercury. Environmental Health Criteria 101. Geneva:World Health Organization, 1990.
10. U.S. EPA. Mercury Study Report to Congress. Washington, DC:U.S. Environmental Protection Agency, 1997.
11. Grandjean P, Weihe P, White RF, Debes F, Araki S, Murata K, Sørensen N, Dahl D, Yokoyama K, Jørgensen PJ. Cognitive deficit in 7-year-old children with prenatal exposure to methylmercury. Neurotoxicol Teratol 19:417–428 (1997).
12. Grandjean P, Weihe P, Nielsen JB. Methylmercury: Significance of intrauterine and postnatal exposures. Clin Chem 40:1395–1400 (1994).
13. Pineau A, Piron M, Boiteau H-L, Etourneau M-J, Guillard O. Determination of total mercury in human hair samples by cold vapor atomic absorption spectrometry. J Anal Toxicol 14:235–238 (1990).
14. White RF, Debes F, Dahl R, Grandjean P. Development and field testing of a neuropsychological test battery to assess the effects of methylmercury exposure in the Faroe Islands. In: Proceedings of the International Symposium on Assessment of Environmental Pollution and Health Effects of Methylmercury, 8–9 October 1993, Kumamoto, Japan. Kumamoto, Japan:Kumamoto University, 1994;127–140.
15. Lezak MD. Neuropsychological Assessment, 3rd ed. Oxford:Oxford University Press, 1995.
16. Wechsler D. Wechsler Intelligence Scale for Children - III. San Antonio, TX:Psychological Corp., 1991.
17. Thorndike RL, Hagen EP, Sattler JM. Standford-Binet Intelligence Scale (Technical Manual). 4th ed. Chicago:Riverside Publ. Co., 1986.
18. Murata K, Weihe P, Renzoni A, Debes F, Vasconcelos R, Zino F, Araki S, Jørgensen PJ, White RF, Grandjean P. Delayed evoked potentials in Madeiran children exposed to methylmercury from seafood. Neurotoxicol Teratol (in press).
19. Davidson PW, Myers GJ, Cox C, Axtell C, Shamlaye C, Sloane-Reeves J, Cernichiari E, Needham L, Choi A, Wang Y, et al. Effects of prenatal and postnatal methylmercury exposure from fish consumption on neurodevelopment. JAMA 280:701–707 (1998).
20. Grandjean P, White RF. Effects of methylmercury exposure on neurodevelopment [letter]. JAMA 281:891 (1999).
21. Goulding M, Smith N, Mahar D. Floods of Fortune: Ecology and Economy along the Amazon. New York:Columbia University Press, 1996.
22. Smith JC, Farris FF. Methyl mercury pharmacokinetics in man: a reevaluation. Toxicol Appl Pharmacol 137:245–252 (1996).
23. Boischio AAP, Cernichiari E. Longitudinal hair mercury concentration in riverside mothers along the Upper Madeira River. Environ Res 77:79–83 (1998).