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Review of neurobehavioral deficits and river fish consumption from the Tapajós (Brazil) and St. Lawrence (Canada)

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Abstract

Our research group is carrying out studies on neurobehavioral changes associated with eating fish from the Upper St. Lawrence River (Québec, Canada) and the Lower Tapajós River (Brazilian Amazon). Here, these studies are reviewed with respect to exposure, effects and intervention. Although mercury (Hg) levels in piscivorous fish are similar in both regions, in the Amazon, fish constitutes the dietary mainstay, while in Quebec, fish consumption is primarily occasional. Mercury exposure of Amazonian fish-eaters was considerably higher than Québec (median blood total Hg: 28 and 1 µg/l, respectively), but fish from the St. Lawrence contain multiple contaminants. For the Tapajós River, increasing hair Hg was associated with reduced motor and visual functions. Comparison of neurobehavioral performance of Québec fish-eaters and non fish-eaters showed a consistent pattern of information processing slowing among the former; these deficits were not related to blood methyl Hg levels. Early changes associated with exposure can be used to trigger intervention. Since fish provide important essential nutrients, mitigation must balance the beneficial and harmful effects. In Canada, advisories from environmental and health agencies consider both these aspects. In the Amazon, we are currently involved in a participatory research whose goal is to reduce Hg absorption, while maintaining fish consumption. © 2002 Elsevier Science B.V. All rights reserved.

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1. Introduction

'The Great St-Lawrence', 'The Mighty Amazon'. These majestic rivers have been used for transport, recreation and nourishment since the first people arrived on their banks. Over the last few hundred years, increasing urban, industrial and agricultural expansion around the St. Lawrence and the lakes and rivers that feed into it, gradually polluted the pristine waters and the flora and fauna within. And even in the presence of current substantial efforts to clean up the St. Lawrence, persistent pollutants, metals and organic compounds, are present in the remaining fish stocks (Environment Canada, 1996). In the Amazon Basin, it is only over the last 40 years that gold mining, with its massive use of mercury (Hg), and colonization practices, leading to deforestation and subsequent leaching of Hg from the denuded soils into the extensive waterways, have con-

taminated the aquatic food chain (Roulet et al., 1998, 1999). Fish, which for many riverine populations, constitute the primary and often sole source of animal protein, are the vehicle for human methyl mercury (MeHg) contamination in this region (Boischio et al., 1995; Dolbec et al., 2001; Lebel et al., 1997).

Methylmercury, like many of the other persistent environmental pollutants that accumulate in fish, is neurotoxic. Our knowledge of their potentially devastating effects on humans comes from environmental disasters, such as the one that occurred in Japan following the dumping of massive amounts of mercury into the Minamata Bay. In 1956, the first cases of severe neurological disorders from Hg poisoning through fish consumption, were reported. Subsequently, thousands of cases were documented among adults, who depended on these fish for food, and mental retardation was described among children, who had been exposed in utero, even when mothers were asymptomatic. Today, persons who were previously asymptomatic are manifesting disorders, increasing the number of victims of this disaster (for a review of Minamata Disease, see:

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Harada, 1995). The same is true for the victims of 'oil disease' that occurred following PCB contamination of cooking oil in Taiwan in 1979, where 2000 persons suffered the immediate effects; recent studies reveal ongoing sequelae (Guo et al., 1999; Yu et al., 2000).

Neurologic disorders and death observed in these catastrophes were subsequent to high levels of toxic exposures. At lower levels of exposure, continued interference with biochemical and cellular processes potentially cause neurophysiological and psychological functions to undergo slow alterations, which, in the early stages, may go undetected due to nervous system plasticity and compensation. Neurobehavioral test batteries, designed to quantitatively evaluate small changes in performance, serve to identify motor, sensory, cognitive and emotional changes in groups of exposed persons, with respect to control groups or to internal or external exposure parameters. The profile of deficits should be consistent with our knowledge from animal and clinical studies of the effects of the particular substance or substances on the brain (Mergler, 1998).

Our research group is carrying out studies on early neurotoxic effects of consumption of potentially contaminated fish from the Tapajós River, a major tributary of the Amazon and the St. Lawrence River. In both studies, exposure to mercury was assessed and cognitive, sensory and/or motor functions were assessed using neurobehavioral test batteries. Here, these studies are reviewed, highlighting similarities and differences with a view to identify further avenues of investigation and intervention.

2. Exposure in the Amazon Basin

To date, we have carried out three studies on populations on neurobehavioral deficits with respect to exposure on riverine populations of the Tapajós river (Lebel et al., 1996, 1997, 1998; Dolbec et al., 2000, 2001). The first study, which served as a feasibility study to assess exposure and determine the face validity of several tests for evaluating neurobehavioral performance, was carried out in the village of Brasília Legal in 1995 and included 37 persons (Lebel et al., 1996). The second study took place the following year in the same village and included 98 volunteers (40% of the adult population) (Lebel et al., 1997, 1998). The third study, which was carried out in the village Cameté included 98 volunteers (Dolbec et al., 2000, 2001). Methylmercury is the sole pollutant that has been identified in this region of the Tapajós River (Akagi et al., 1995a; Kehrig et al., 1997, 1998a,b; Lebel et al., 1997; Malm et al., 1995). Although pesticides, used in agricultural and for the control of insect-borne diseases, may also be present, a recent study shows only trace levels of organophosphates in fish (Soumis, unpublished data).

In this particular region of the Tapajós River Basin, fish consumption is the only source of human Hg exposure, contrary to areas around gold-mining and refining where populations are exposed to mercury vapors (Branches et al., 1993; Akagi et al., 1995b; Palheta and Taylor, 1995). For many families fish is eaten daily. Fig. 1 shows the distribution of hair total Hg levels from the three studies that were performed by our research group, which surveyed 233 persons, aged 15 years and over (Lebel et al., 1996, 1998; Dolbec et al., 2000). Median total Hg level is 11 $\mu\text{g/g}$ and 80% of the population have levels that surpass 6 $\mu\text{g/g}$; the outliers are fishermen who report high levels of consumption of carnivorous fish. These data are similar to those obtained in other studies in this same region, and in other areas of the Amazon (Akagi et al., 1995a; Boischio et al., 1995; Barbosa et al., 1997, 1998; Cordier et al., 1998; Kehrig et al., 1997, 1998a,b; Leino and Lodenius, 1995; Malm et al., 1995).

In our studies in the Amazon, diet was surveyed with respect to quantity (number of fish meals) and fish species, which were later grouped into categories: herbivorous, carnivorous; omnivorous. Hair mercury levels varied with fish intake and with the type of fish consumed (Lebel et al., 1997; Dolbec et al., 2001). Longitudinal sequential analysis of 24 cm of women's hair (26 women from one village and 36 from a second village) showed seasonal variations that reflect the availability of different fish species (Lebel et al., 1997; Dolbec et al., 2001). In the study in Cameté, we were able to conserve blood samples and assess total mercury concentrations ($n = 96$); levels varied from 9 to 115 $\mu\text{g/l}$; median: 28 $\mu\text{g/l}$ and were highly correlated ($r = 0.82$) to hair total mercury (Dolbec et al., 2000). In this study, we were unable to determine blood methylmercury concentrations.

3. Exposure in the Upper St. Lawrence Basin

Our study on the population from the St. Lawrence did not originally set out to examine the effects of fish consumption. The data comes from a study of manganese neurotoxicity among persons living on the south shore of the Upper St. Lawrence River, where eating fish from fluvial lakes of the Upper St. Lawrence was surveyed as a potential confounding variable (Mergler et al., 1999). In this survey, 117 (39.5%) of 296 persons, selected using a random, stratified sampling strategy, responded positively to a question on whether they ate fish from Lake St. François and Lake St. Louis (Mergler et al., 1998). Analyses of blood Hg levels for this population showed that total Hg was significantly higher (Mann–Whitney: $P < 0.01$) among fish eaters compared with non fish eaters: median: 1 $\mu\text{g/l}$, ranging from 0.10 to 4.8 $\mu\text{g/l}$ versus 0.8 $\mu\text{g/l}$, ranging from non

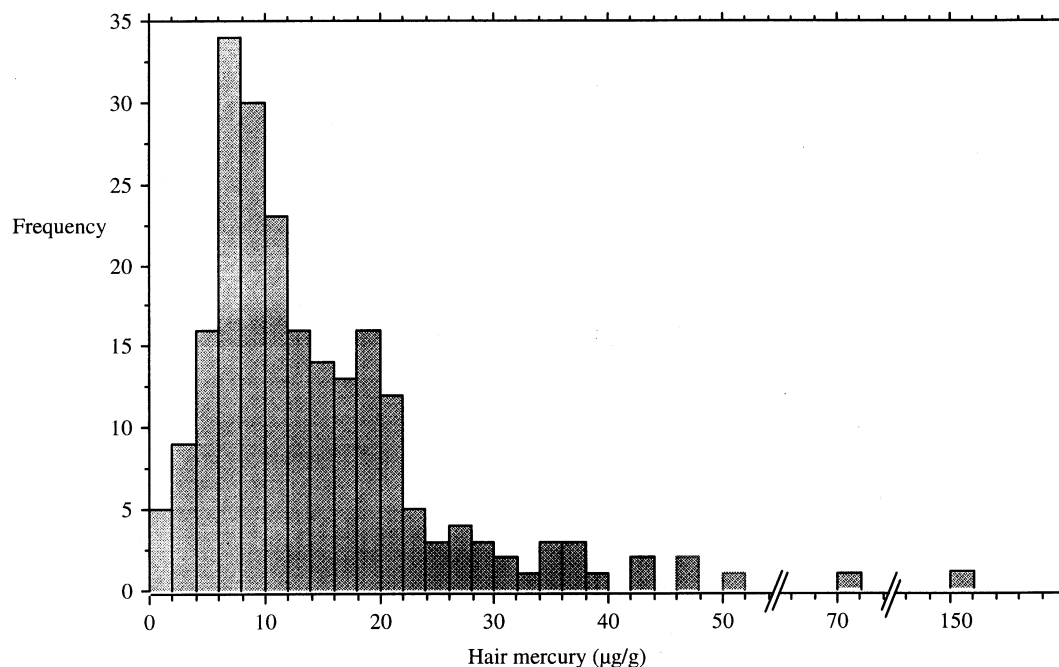


Fig. 1. Total hair mercury levels for three riverside populations ($n = 233$) living along the Tapajós River, a major tributary of the Amazon.

determinable to 0.10–4.21 $\mu\text{g/l}$). This was due to differences in organic mercury levels which were significantly higher (Mann–Whitney; $P < 0.001$) among the fish eaters (median: 0.70 $\mu\text{g/l}$) compared with the non-fish eaters (median: 0.40 $\mu\text{g/l}$), while no differences were observed for inorganic mercury (Mahaffey and Mergler, 1998). We did not measure hair mercury levels in this study.

Blood MeHg levels increased with increasing fish consumption (Kruskall–Wallis: $P < 0.0001$); the median value for those who reported eating fish in only one season being 0.60 $\mu\text{g/l}$, while for those who ate the fish throughout the year, it was 0.80 $\mu\text{g/l}$. There was a positive correlation between the number of fish meals and blood MeHg (Spearman's- r : 0.36; $P < 0.0001$). It is interesting to note that blood lead (Pb) likewise was significantly higher (Mann–Whitney; $P < 0.0001$) among fish consumers compared with non-consumers (3.73 vs. 2.90 $\mu\text{g/dl}$). In this study, which was not specifically designed to examine fish consumption, we did not obtain measures of hair mercury, nor of the other known contaminants, such as PCB congeners, Mirex, DDT and DDE, that have been identified in fishermen in this region of the St. Lawrence (Kosatsky et al., 1999).

4. Neurotoxicity in the Amazon Basin

The average age of the Amazonian villagers who participated in the studies of nervous system functions was 33 years (S.D.: 15), ranging from 15 to 81 years. Fig.

2 provides the age distribution for the men and women. The distribution is similar to that of the entire populations of these villages. There is a drop in the relative frequency of men between 34 and 45 years due to the fact that many leave the village to seek work elsewhere.

Since animal and clinical studies indicate that MeHg affects motor and visual performance (Harada, 1995; Evans et al., 1977; Rice and Gilbert, 1982, 1990; Rice, 1989; Sakamoto et al., 1993; Spyker et al., 1972), we designed a neurobehavioral test battery to evaluate these functions in a setting that did not have electricity and for a population with little formal education. A feasibility study, carried out in 1995, showed that the tests were culturally acceptable and varied as expected with age and education (Lebel et al., 1996); all tests were administered in Portuguese by trained University students from a local outreach campus of the Federal University of Para. Table 1 contains a list of the tests that were used in the Tapajós River study. In all villages, manual dexterity was evaluated using the Santa Ana Test (Helsinki version), grip strength and fatigue were assessed with a dynamometer and visual acuity, color vision and visual contrast sensitivity were evaluated using charts for near and far vision, the Lanthony D-15 desaturated test, and the Vistech 6000, respectively. Fine motor movement and speed, measured using the Grooved Pegboard and the Fingertapping Test were included in last study. The testing procedures are described in Lebel et al. (1998), Dolbec et al. (2000). In addition, a randomly selected sub-group of 117 persons underwent a neurological examination, including the motor coordination task, the Branches Alternate

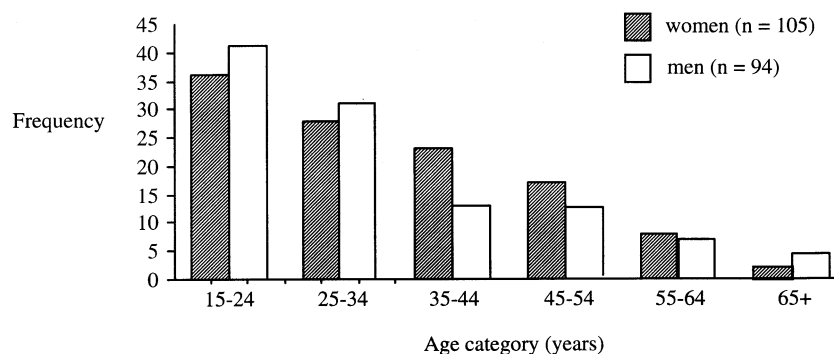


Fig. 2. Age distribution of the Tapajós population who participated in neurofunctional assessment studies.

Movement Task (BAMT), described in [Lebel et al. \(1998\)](#).

The overall results are presented in [Table 1](#). Fine motor movement and dexterity were most sensitive to mercury exposure and decreased significantly with increasing total hair mercury, taking into account age, educational level and other factors that could influence performance outcome ([Lebel et al., 1996, 1998; Dolbec et al., 2000](#)). No consistent dose-effect relations were observed for grip strength or for fatigue measured with a dynamometer. Near visual contrast sensitivity decreased with increasing hair total mercury concentrations among those under 35 years ([Lebel et al., 1998](#)). The neurological examination in the sub-population examined was, for the most part, normal, although there was a high prevalence of hyperreflexia (45.3%), reduced visual field (41.0%) and disorganized movements on the BAMT (36.8%). Only the latter varied with hair mercury levels, increasing from 27.4% ($n = 26$) for those with hair mercury levels $< 20 \mu\text{g/g}$ to 77.2% ($n = 17$) for those whose hair Hg levels were $\geq 20 \mu\text{g/g}$. The Odd's Ratio for disorganized movements at hair Hg levels $\geq 20 \mu\text{g/g}$ was: 9.02 (3.02–26.9). In all cases, the regression model using hair total mercury was more significant than the model with hair methyl mercury or blood mercury.

5. Neurotoxicity in the St. Lawrence Basin

In the study on the Upper St. Lawrence, the test battery was much more extensive covering cognitive, sensory and motor functions ([Table 1](#)). All participants underwent a neurological examination. The test battery is described in detail in [Mergler et al. \(1998\)](#).

Multiple regression analyses, including age, educational level, smoking, alcohol consumption as co-variables, revealed no differences between fish-eaters and non fish-eaters on tests of sensory function, visual memory and recognition, fine motor performance and some motor tests. However, fish-eaters performed significantly more poorly ($P < 0.05$) on tests requiring

cognitive flexibility, word naming, auditory recall, and more complex motor tasks. Although fish-eaters and non-fish-eaters were similar for most socio-demographic variables, significantly more fish-eaters (65.2%) reported consuming alcoholic beverages as compared with non-fish-eaters (42.4%) ($\chi^2 < 0.01$) ([Mergler et al., 1998](#)). To eliminate this possible bias, further analyses were performed using matched pairs. For these analyses, fish-eaters were matched to non-fish-eaters for the variables sex, alcohol consumption (never or occasionally vs. regularly), age (± 5 years) and education (± 2 years). A total of 63 matched pairs were thus created. Results were unchanged from those obtained using multiple regression analyses with the entire group ([Mergler et al., 1998](#)).

The profile of differences between the St. Lawrence fish-eaters and non fish-eaters is interesting ([Table 1](#)). In tests, such as Digit Span Forward and Backward, where one is required in the first part to repeat numbers in the same order as they are presented and, in the second part, to repeat them in the inverse order, the difference between the non fish-eaters and fish-eaters was just at significance level ($P = 0.05$) for the former, but highly significant ($P < 0.01$) for the latter. For the Trailmaking Test, the same phenomenon was observed: in the first part (Trailmaking A) where one is required to draw a line linking numbers, randomly distributed on a sheet of paper, in ascending order, there was no difference between fish-eaters and non fish-eaters; however, when the test required set shifting, going from a number to a letter and back to a number (1-A-2-B-3), the differences were very significant ($P < 0.01$). This pattern was similar for the Switching Attention Test and for different tasks on the neurological examination, where no differences were observed for simple movements, while fish-eaters were significantly slower on the more complex BAMT. This overall profile of deficits is consistent with slowing in information processing.

Although fish-eaters had higher levels of blood organic mercury and lead, no dose-effect relations were observed between these bioindicators of exposure and neuro-outcomes.

Table 1
Comparison of results from neurofunctional testing in the studies on the Tapajós and St. Lawrence rivers

Test	Tapajós study	St. Lawrence study
<i>Auditory learning and/or recall</i>		
List acquisition and recall (memory assessment scale)	–	*
Digit span test	–	*
<i>Cognitive flexibility</i>		
Stroop color word	–	*
<i>Grapho-motor tests</i>		
Trail-making A	–	ns
Trail-making B	–	*
Cancellation H	–	*
<i>Visual recognition & recall</i>		
MAS visual recognition and recall	–	ns
Rey 15 item memory test	–	*
<i>Reaction time tests (NES-2)</i>		
Continuous performance	–	ns
Switching attention	–	*
<i>Fine motor movements and dexterity</i>		
Fingertapping test	*	ns
Grooved pegboard	*	–
Purdue pegboard	–	ns
Santa Ana (Helsinki version)	*	–
Neurological motor examination		
Distal motor events	–	ns
Proximal motor events	–	ns
Branches alternate movement task (BAMT) ^a	*	*
<i>Muscle strength</i>		
Grip strength (dynamometer)	ns	–
Fatigue (dynamometer)	ns	–
<i>Sensory tests</i>		
Near visual acuity	ns	ns
Near visual contrast sensitivity	*	ns
Color vision (Lanthony D-15 desaturated)	*	–
Olfactory threshold (ds)	–	ns

For the Tapajós study, (*) indicates a significant dose-effect relation with hair total mercury and for the St. Lawrence Study (*) indicates a significant difference between fish-eaters and non fish-eaters; (ns) test administered, but results not significant; (–) test not administered.

^a The response recorded for the Branches Alternate Movement Task in the two studies were different: For the Amazonian study, disorganized movement was noted while for the St. Lawrence Study, the time to perform the task 20 times in succession was recorded.

6. Discussion

For the riverine populations from both the Tapajós and the St. Lawrence, there was an association between fish-eating and mercury exposure. Blood mercury concentrations were over 25 times higher on the Tapajós as compared with the St. Lawrence, probably reflecting the higher quantity of fish consumed by this population. Indeed, on the Tapajós, many families eat fish daily and all eat fish at least several times a week, while on the St.

Lawrence, eating fish from the river is mostly occasional. There was, however, one participant in the St. Lawrence River study who was a subsistence fisher and ate fish on a daily basis (Mahaffey and Mergler, 1998); his blood mercury level was 70 µg/l which corresponds to the upper 90% of the Tapajós River population. In the Amazon, concentrations in this range were observed among fishers and their families who ate fish at almost every meal and reported a preference for piscivorous fish. No contaminants other than mercury were assessed for the Amazonian population since there is no evidence of other sources of pollution in this region. In Québec, studies from this same area have shown that sportfishers who are high consumers of the fish they catch have higher levels of persistent organic pollutants, such as PCB congeners, DDT, DDE and Mirex compared with fishers who eat less of their fish (Kosatsky et al., 1999). In the present St. Lawrence study, blood Pb levels likewise increased with increasing fish consumption. Other studies from the Great Lakes and the St. Lawrence have made similar observations (Schantz et al., 1999; Kosatsky et al., 2001). Results from Kosatsky et al. (2001) suggest that consumption of game waterfowl may explain this relation.

In both of the riverine populations that we studied there was evidence of neurofunctional deficits associated with fish-eating practices. For the Tapajós, this was reflected in the dose-effect relations between hair total mercury levels and neuro-outcomes, while for the St. Lawrence, this was reflected in the differences between fish-eaters and non fish-eaters. There were however, different patterns in the profile of deficits. For those from the Tapajós river, loss of fine motor capacities, coordination, manual dexterity and visual functions were related to hair total mercury levels. These findings are consistent with studies on pre and postnatal methylmercury exposure in monkeys (Rice and Gilbert, 1982, 1990; Rice, 1989, 1996). In our Amazon studies, cognitive tests were not administered due to the low level of formal schooling and cultural differences; thus, it is not possible from these studies to ascertain whether there is an association between exposure and cognitive capacities in this population. Grandjean et al. (1999) reported dose related neurobehavioral deficits with Hg exposure among children from villages along the Tapajós River. Those with higher level of hair mercury presented decrements on tests of motor function, attention, and visuospatial performance.

The profile of deficits for the St. Lawrence population, was consistent with slowed information processing. No differences were observed on simple tasks, but as the tasks become more complicated involving set shifting differences became apparent. Differences were also observed on auditory recall and delayed recall. Contrary to the Tapajós participants, fish-eaters and non fish-eaters from the St. Lawrence performed similarly on

tasks involving fine motor movement and near visual contrast sensitivity. Unlike the Tapajós, there is a multitude of contaminants in fish in the St. Lawrence (Environment Canada, 1996). Indeed, a large number of organic pollutants and metals have been associated with consumption of fish from this area (Kosatsky et al., 1999). Although taken individually, each one may be inferior to accepted permissible levels, the body burden for neurotoxicity may be sufficient to produce the changes that we observed. Kosatsky reported high levels of the PCB, Arochlor 1260, among high sports fish consumers (Kosatsky et al., 1999) compared with low fish consumers. In a study of neurobehavioral performance in older (49–86 years) fish-eaters and non fish-eaters from Lake Michigan, Schantz et al. (2001) reported an inverse relation between PCB exposure and scores on several measures of memory and learning, including a similar test of auditory learning and recall to the one used here. In the present study, we cannot attribute the deficits to any particular substance; no relation was observed between blood MeHg and any of the outcomes. Rice (1995) has aptly pointed out that most of the contaminants found in the Great Lakes and the St. Lawrence have neurotoxic properties. Studies need to be designed to examine not only the consequences of each substance separately, but possible synergistic, inhibitory or additive effects.

There was no frank illness associated with the consumption of contaminated fish from either the Tapajós or the St. Lawrence Rivers. There are, however, significant changes in several domains of neurobehavioral and neurophysiological performance. The profile of changes suggests that the observed effects result from exposure to different contaminants, or in the case of the St. Lawrence, possibly contaminant mixtures. Early alterations may be particularly important at the moment of formation and decline of the nervous system when even small changes can have major effects (Weiss, 1996; Adams et al., 2000). Small shifts in neurobehavioral performance may be indicative of diminished well-being in the exposed population. For example, decreased manual dexterity, fine motor movements and vision for a fisher from the Amazon may mean that he or she will be less capable of repairing nets; this activity would take longer and thus leave less time for fishing. Decreased information processing may have important consequences in an aging population. Further studies should focus on the relation between early deficits and quality of life.

Early changes in neuropsychological and neurophysiological functions associated with exposure parameters can be useful triggers for public health and environmental intervention. For contaminants transmitted to humans through fish consumption, intervention strategies need to consider the health benefits resulting from fish-eating. Fish are an excellent dietary source for many

essential elements and for the Amazonian population, the major and often only source of animal protein. Thus, any proposal for diminishing exposure should be based on a good knowledge of the aquatic ecosystem, the source(s) of pollution, and the social, cultural and economic aspects of the diet. In Canada and the US, fish advisories serve to inform the population and limit intake of potentially contaminated fish, while public health authorities provide information on the benefits of fish consumption. An interdisciplinary network of Canadian researchers (Collaborative Mercury Research Network (COMERN)) has just begun a major 5 year study of the sources, transmission and health impact of mercury from an ecosystemic and participatory research perspective. In the Amazon, we are currently involved in a pilot project in a village on the Tapajós River, whose goal is to work with the community to reduce mercury absorption while maintaining fish consumption. The project focuses on three aspects: (i) diet (short term); (ii) 'hot spots' or areas that are propitious to methylation in the areas of fish capture (medium term) and (iii) reforestation to diminish Hg leaching (long term). Follow-up studies of this group will allow us to determine whether the observed deficits are reversible, progressive or stable over time.

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