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Serum PCBs and Blood Mercury as Indicators of Human Health in Upper Laurentian Great Lakes

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ABSTRACT

Background: The Ojibwe Health study conducted between 1994-2003 assessed blood mercury (bHg) and serum polychlorinated biphenyls (PCB) burdens in 291 participants from 9 tribal reservations in the upper Great Lakes region of the United States.[1] This paper presents a post-hoc analysis to further explore contaminant health effects using bHg and PCBs as exposure indicator variables and further explored the variation in exposure patterns for the tribes.

Methods: The association between chemical concentrations and the fish consumption variables were tested in backwards multiple linear regressions with individual fish consumption variables as the main independent variable and the chemical concentrations as the dependent variable. Logistic regressions were performed post-hoc on the original dataset using bHg and serum PCBs separately as independent variables. These independent variables were regressed with 40 self-reported health conditions.

Results: There were significant associations between blood Hg, PCBs, and the fish consumption variables by tribal region. Except for diabetes and allergies, associations between contaminants and health outcomes were lost after accounting for age, though suggestive associations with numbness/tingling reappeared after controlling for age and other confounders.

Conclusion: Tribal exposure to PBTs from fish consumption is overall similar to the general population, however, different consumption patterns within tribes leads to varying levels of exposure. Adult health outcomes were not strongly associated with exposure variables, except diabetes, which merits a more in-depth investigation designed to explore the interplay between obesity, lipids, PCBs, and metabolic disorders. Updated biomonitoring efforts for this population are highly necessary to provide useful dietary guidance.

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Background

This article presents a retrospective study of the evidence regarding environmental exposures to persistent bioaccumulative toxic (PBT) chemicals gathered during the Ojibwe Health Study (OHS). During the OHS, tribal consumption data and biological samples were collected in 1993 through 2000 then analyzed in 2003 by the Division of Laboratory Sciences at the National Center for Environmental Health (NCEH) of the CDC for whole blood mercury (bHg) in ppb (μg/L) and serum PCBs in ppb (μg/L). The Ojibwe include 18 federally recognized individual tribes in the states of Minnesota, Wisconsin, and Michigan. The Ojibwe tribes harvest both fish and wild rice for personal and commercial purposes. These tribes reside in the Upper Laurentian Great Lakes (GL) and share a common cultural identity, which includes subsistence on fish, but reside within distinguishable GL regions. Many of these tribes live along the shores of Lakes Superior and Michigan, although some are located inland from the GL and use primarily smaller freshwater lakes as their fisheries, often walleyed pike (Stizostedion vitreum). These regions were previously reported to display varying fish consumption patterns which could influence their exposures to PBTs relative to one another.[1] This notion, along with epidemiological evidence collected during OHS but never published, is evaluated here to articulate the future priorities for environmental research in this region - twenty years after the initiation of OHS.

The most common route of human exposure to Polychlorinated Biphenyls (PCBs), mercury (Hg) and many other PBTs is contaminated fish in the diet.[2] Dietary exposure from fish consumption is a major concern to many people throughout the world-especially fishing communities with long traditions for both subsistence and commercial dependence upon their fisheries.[1,3] This concern persists from recent decades regarding the presence of PBT chemicals in the GL. Native American tribes may be particularly vulnerable to PCB and Hg due to their propensity to bioaccumulate within subsistence food chains[1,3] and because of their known toxic effects when humans are exposed to high concentrations.[4-6] National Health and Nutrition Examination Survey (NHANES) data suggests that exposure from Hg, at least, are higher for "Asian, Pacific Islander, Native American, or multiracial".[7,8] It is unclear, however, to what extent this reflects the Ojibwe diet versus other cultures who eat higher amounts of ocean fish that may contain elevated Hg levels.[7] Misclassification, underrepresentation, and a general lack of data regarding Native American health in large datasets such as NHANES are a prominent problem.[9-11] This limits the interpretability of public health interventions such as state-sponsored fish consumption advisories.

Many states in the U.S. have published fish consumption health advisory information aimed at warning fishers and their families about the potential health risks associated with eating fish contaminated with PBT chemicals.[12] The International Joint Commission's Health Professional Advisory Board (IJC/HPAB) summarized the status of both the risks and the benefits related to eating GL fish containing mercury and PCBs.[13] Similarly, The World Health Organization's (WHO) 53rd Joint FAO/WHO Expert Committee on Food Additives concluded that certain populations and ethnic groups must weigh the nutritional benefits against the possibility of harm to the developing fetus when mercury contaminated fish are consumed.[14] The International Joint Commission (IJC), along with many other organizations, officially recognizes the benefits of fishing activities and fish consumption including: (1) important nutrients, (2) aesthetic social activity, and (3) economic activity. Furthermore, fish advisories should be cautious about encouraging traditional fishing cultures from switching to more harmful diets that may in fact pose as much or more risks.[13] Susceptible populations such as pregnant or nursing mothers must be provided with appropriate education and safe choices to help reduce their exposures to harmful contaminants which can affect fetuses, infants and young children.[12]

Though the most prominent health effects of methylmercury poisoning in humans are the developmental neurotoxic effects in children,[6,15] adults also experience clinical effects at acute exposures.[2] The predominant concerns for Hg exposures in adults include cardiovascular disease, autoimmune disease, infertility, neuropsychiatric effects, and subjective complaints.[7] Furthermore, many of these adverse health effects may occur at mercury levels previously thought to be safe.

The toxic effects of PCBs in animal studies have included neurobehavioral effects, hormonal effects and immune system suppression.[16-21] In 1972, 1,057 people were acutely poisoned by eating rice oil contaminated with PCBs in Japan, and 11% of those exposed suffered jaundice.[4] Despite the large body of literature on potential associations between early-life exposure to PCBs and adverse neurodevelopmental effects, controversy still exists over whether PCBs are in fact neurotoxicants.[22] Health effects from doses seen in the general population are not consistently documented [22, 23] except for the hypothesized link between Diabetes and PCBs.[24-27]

Fish consumption, Great Lakes or otherwise, results in multiple exposures from a variety of PBT chemicals. The very presence of so many factors raises a problem of multiple comparisons. It is possible, however, to conceptualize risk in terms of consumption advisories. In the Great Lakes, most state-level advisories are based on PCBs and Hg; these are the chemicals that tend to exceed minimum risk levels at typical consumption rates.[12] From a consumption standpoint, the consumer is armed with information to avoid these chemicals more so than others (except perhaps dioxins). If the consumption advisories alter behavior based on Hg and PCB risk, then these biomarkers may describe the health consequences of either avoiding or adhering (perhaps inadvertently) to consumption advisories. Therefore, we analyzed the associations between bHg, PCBs, select confounders from OHS, and self-reported health histories (checklist of 40 items) in Ojibwe adults.

Table 1. Self-reported chronic disease and symptoms gathered from a 12 page questionnaire. To evaluate chronic disease and other health conditions, study physicians created disease and symptoms check lists in the survey for a total of 40 health conditions of relevance. A. Twenty-one health conditions based upon the statement, "Have you ever been told by a doctor that you had any of the following?" B. Nineteen symptoms queried by asking, "Have you experienced any of the following health conditions?"

+Smoking significant affect (p=0.043) on Heart Disease confirmed.
++Alcohol significant affect (P=0.036) on miscarriages.

Doctor's Diagnosis	Self–reported Symptom
Hay Fever or Allergies	Burning or Itching Skin
Arthritis or Rheumatism	Frequent Chest Colds
Asthma	Frequent Head Colds
Bowel Disease	Coordination Difficulty
Cancer	Coughing Spells
Emphysema/Bronchitis	Cough Blood
Diabetes	Discharge / Swollen Eyes
Ear Infections	Dizziness or Fainting
Epilepsy or Seizures	Eye Pain or Itching
High Blood Pressure	Fatigue
Heart Disease +	Headaches
Infertility	Joint Pain
Kidney Disease	Memory Loss
Liver Disease	Numbness or Tingling
Migraine Headaches	Phlegm from Coughing
Miscarriage ++	Rashes or eruptions
Skin Allergies or Diseases	Shaking or Tremors
Thyroid or Goiter	Blurred Vision
Ulcer GI	Difficulty with Coordination
Birth Defects	Neurological Disorders

Our previous OHS reports have shown that the fish collected and consumed by these tribes are moderately contaminated with mercury, PCBs or both.[3,28-30] In the current paper, the data from the cross-sectional epidemiologic study[1] were evaluated for any associations (positive or negative) between tribal fish consumption and self-reported chronic health outcomes in adults. The results provide insight regarding the extent to which consumption of contaminated fish increases the risks of adult disease. Additionally we confirmed the a-priori assumption[1] that Ojibwe tribes experience different exposure patterns based on the source of fish they consume. This guides our research as we consider future possibilities of biomonitoring and tribal-relevant consumption advisories in the region.

Methods

Subjects, Questionnaires, and Study Sites: The OHS was a cross sectional study of participants from Nine Ojibwe tribes. Much of the methods summarized here are described in earlier papers.[1,28] Most subjects were recruited at tribal health fairs. Serum samples were solicited from approximately half of the 822 OHS participants. A twelve page questionnaire (revised in 1995) was used to gain information regarding the demographic variables, self-reported chronic disease and symptoms, fish consumption, lifestyle, and exposure variables. To evaluate chronic disease and other health conditions, study physicians from the Medical College of Wisconsin's Department of Preventive Medicine created disease and symptoms check lists in the survey for a total of 40 health conditions of relevance (Table 1). Twenty-one questions were based upon the statement, "Have you ever been told by a doctor that you had any of the following?" Then 19 symptoms were queried by asking, "Have you experienced any of the following health conditions?"

Blood Hg Analytical Method: Whole-blood specimens were analyzed for both total mercury and inorganic mercury. Specimens were analyzed using automated cold-vapor atomic-absorption spectrophotometry by the Division of Laboratory Sciences at the NCEH. The detection limit was 0.14 mg/L for total mercury and 0.4 mg/L for inorganic mercury. Mercury was measured by Flow Injection Mercury System 400 (Perkin–Elmer, Shelton, CT) with an AS-91 autosampler. All solutions were made of analytical-grade chemicals. Ultrapure water at 3–18MO (Milli-QTM, Millipore Corp. Bedford, MA, USA) was used for solution preparation. Matrix-matched calibration methods were used. All blood samples were kept frozen from the time of aliquoting until the analysis. The total blood mercury analysis utilized a Maxidigest MX 350 (Prolabo, Fontenay-sous-Bois, Cedex, France) in-line microwave digester connected to the FIMS-400 system. The inorganic mercury analysis utilized stannous chloride as the reducing agent, and the total mercury analysis utilized sodium borohydride as the reducing agent. The blood mercury analysis required 0.2mL of blood for the total and an additional 0.2mL of blood for the inorganic analysis.

For both total and inorganic mercury measures, National Institute of Standards Technology Standard Reference Material (NIST SRM 966) was used as a bench quality-control material as well as three levels of in-house blood pools traceable to NIST SRM 966 for daily quality control. One of two different levels of a blind quality-control material was inserted in every analytical group of samples for an additional quality-control check. All quality-control specifications were met in the analyses of the samples.

Blood PCB Chemical Analytical Method: Serum samples from the ATSDR/OHS project were submitted to the NCEH for analysis using isotope-dilution mass spectrometry (IDMS). The new IDMS method provides profiles very similar to that reported for the GLPF project.[30] Briefly, the differences between the serum organochlorine methods for our GLPF study and the CDC NCEH analyses were as follows: The GLPF project used 10mL of serum from 61 participants to quantify 93 peaks for

126 congeners using Hewlett–Packard (Palo Alto, CA, USA) Model 5880A with a DB-5 capillary column and electron-capture detection (ECD) following the basic modified methods of Mullin as published in Gerstenberger et al.[30,31]

For the OHS project, 307 participants' (included 38 nontribal spouses and nonnative tribal employees for comparison purposes) serum samples were shipped to the NCEH for analysis using the IDMS method.[32] PCBs were analyzed using high-resolution gas chromatography/isotope-dilution high-resolution mass spectrometry. Serum samples were spiked with 13C12-labeled internal standards, and the analytes of interest were isolated using either a C18 solid-phase extraction or a liquid–liquid extraction procedure followed by a multicolumn automated clean-up and enrichment procedure. The analytes were chromatographed on a DB-5 MS capillary column (30m_0.25mm_0.25 mm film thickness) using selected ion monitoring at a 10,000 resolving power using either a Micromass Autospec ULTIMA or Finnigan MAT95 mass spectrometer in the EI mode.

The concentration of each analyte was calculated from an individual standard linear calibration. Each analytical run was conducted blind and consisted of three unknown serum samples, a method blank, and a quality control sample. After all data were reviewed using comprehensive quality assurance/quality control procedures, the analytical results were reported on both a whole-weight and lipid-adjusted basis. Serum total lipids were determined using an enzymatic ''summation'' method. Detection limits, on a whole-weight basis and a lipid-adjusted basis, were reported for each sample and corrected for sample weight and analyte recovery. All human serum specimens were handled using universal precautions.

A previous OHS report demonstrated that lipids only significantly correlated with 12 of the 36 PCB congeners.[33] The Schaeffer report[33] further raised questions as to the validity of assuming that lipid profiles predispose PCB partitioning into serum. Given the low correlation for this group and the doubts regarding the causal vs coincidental nature of serum lipids and PCBs, the current study used unadjusted serum PCBs to as the fish contamination risk factor.

Statistical Analyses: Univariate ANOVAs were conducted to detect differences among the tribal regions for the average amount of each source of fish that was eaten by tribal members. As a confirmation of the original *a priori* testing reported in Dellinger,1 the association between chemical concentrations and the fish consumption variables were tested in backwards multiple linear regressions with individual fish consumption variables as the main independent variable and the chemical concentrations as the dependent variable.

Table 2. Tribal Regions Mean and Standard Deviation Fish Grams/Year by Source. The number of respondents who reported eating fish from that source is indicated in parenthesis.

Group	Inland Lakes * X ±	L. Superior ** X ±	L. Michigan *** X ± SD (N)	Restaurant **** X ± SD (N)	Store X ± SD (N)
Lakes Michigan, Huron & Superior (MHS)	3041 ± 8259 (166)	5012 ± 8369 (163)	4274 ± 12279 (198)	3813 ± 8681 (188)	3450 ± 12442 (183)
Lake Superior (LS)	2918 ± 6815 (325)	6538 ± 11121 (327)	424 ± 2222 (322)	2662 ± 7134 (324)	2861 ± 8155 (324)
Inland Lakes (IN)	11246 ± 20493 (48)	1031 ± 3174 (31)	204 ± 695 (30)	3399 ± 6648 (36)	1048 ± 2752 (36)
Non-Ojibwe (NO)	13742 ± 16109 (36)	850 ± 821 (4)	1921 ± 1976 (10)	2537 ± 3037 (20)	4025 ± 4769 (14)
Other Ojibwe Res (OR)	6649 ± 15052 (40)	2498 ± 5156 (42)	6288 ± 15684 (53)	7313 ± 13417 (50)	4705 ± 9531 (44)

*Significant differences among Tribal Regions $F_{(4,610)}$ =15.76, p<.001.

**Significant differences among Tribal Regions $F_{(4,562)}$ =3.90, p=.004.

***Significant differences among Tribal Regions $F_{(4,608)}$ =9.89, p<.001.

****Significant differences among Tribal Regions $F_{(4,613)}$ =3.68, p=.006.

Regarding the self-reported health conditions, associations between chemical concentrations and self-reported medical history items were examined in backwards multiple Logistic regression analysis with the individual chemical concentration variables as the main independent variable and the individual medical history items as the dependent variables. Potentially confounding variables (including demographic variables and various exposures) were included as independent variables in the regression equation if they demonstrated a statistically significant association ($p<0.05$, two tailed) with the chemical concentration variables in univariate analysis (Student t-test or Chi square test). Potential confounding variables included: BMI, alcohol, amalgams, medicated shampoos, and smoking in pack-years. The independent variables of Gender and Age were included. Due to multiple comparisons (four families of tests with about 20 observations each) an exploratory value of $p<0.025$ was considered significant and suggestive results of $p<0.054$ were noted.

Results

Fish Consumption: The *a-priori* assumption[1] that the tribal groupings used to characterize fish consumption patterns for OHS exhibit significant differences between groups in their sources of fish was confirmed (Table 2). There were significant associations between blood Hg and the fish consumption variables by tribal region. Scheffé *post-hoc* tests indicate that the IN (Inland) tribal members and the NO (Non-Ojibwe) tribal members had significantly higher concentrations of blood mercury than the MHS tribal members ($p=0.04$ and $p=0.017$, respectively), and these groups are more likely to consume panfish, bass, and walleye rather than the tribes associated with GL fisheries GL shoreline tribes.

PCB concentrations varied greatly by tribal grouping ($F_{(4,263)}=5.132$, $p<0.001$), with the Michigan-Superior (MHS) group exhibiting the highest concentrations. Scheffé post-hoc tests indicate that the MHS participants had significantly higher concentrations of blood PCBs than the Non-Ojibwe ($p<0.001$) and Inland groups ($p=0.033$). PCB concentrations showed a positive association with whitefish ($\beta=0.178$, $p=0.025$) and an inverse relationship with walleye ($\beta= -0.191$, $p=0.02$) consumption. This suggests whitefish were a more likely source of PCBs than Walleye. There was a positive association between PCB serum concentrations and Lake Michigan fish consumption ($\beta=0.41$, $p=0.043$).

Blood Hg concentrations: There were 307 tribal volunteers, whose blood samples were analyzed for total Hg concentrations, including nine whose values were below the lowest detectable limit of 0.14 µg/L. These individuals were assigned a value of 0.07 µg/L (one-half of the lowest level of detection). The mean total blood mercury level by subject was 1.52 µg/L, with a maximum of 11.8 µg/L. The upper 95th percentile was 4.67 µg/L, which was similar to the NHANES data (also NCEH

Table 3. Fish Consumption by Tribal Region (Ojibwe groups in italics) rank ordered by Highest to Lowest Fish Consumption and Lowest to Highest self-reported Allergy, Diabetes and Cancer.

Tribal Group	Fish(g/day) Mean(Medn)	Allergy	Diabetes	Cancer	Heart Disease	Liver Disease
OtherOjibweRes *(OR) N=76*	87 (27.3)	10.5%	10.3%	2.6%	2.6%	5.2%
Lakes Michigan, Huron & Superior *(MHS) N=271*	62 (29.6)	12.9%	10.0%	2.6%	5.5%	0.4%
Lake Superior *(LS)N=346*	60 (29.8)	14.5%	15.1%	4.4%	5.8%	1.5%
Inland Lakes *(IN)N=63*	46 (20.0)	20.6%	19.0%	4.8%	4.8%	0.0%
Non-Ojibwe (NO)N=66	34 (21.4)	19.7%	8.5%	4.2%	1.4%	0.0%
All Tribal Participants N=822*	**60 (26)**	**14.5%**	**12.7%**	**3.6%**	**5.0%**	**1.2%**
Cases or Samples	N = 720	N=119	N=105	N=30	N=41	N=10

*Based on all 822 participants completing questionnaires.

Table 4. Odds Ratios (95% CI) for Self-Reported Health Disorders based on doctor's diagnoses or symtpoms by total Polychlorinated Biphenyls in serum (PCBs), total whole blood Mercury (bHg). Gender differences were checked and did not change the main effects. *Suggestive differences in Logistic Regression p<0.054. **Significant differences in Logistic Regression p<0.014. ***Significant differences in Logistic Regression p<0.001. Confounders tested were: Alcohol, Silver Amalgams, Medicated Shampoo, and Years of Smoking (Packyears)

Diagnosed Condition	PCBs	PCBs Age	PCBs Confounders	bHg	bHg Age	bHg Confounders
Hay Fever or Allergies	0.94 (.800-1.108)	0.95 (.792-1.142)	1.03 (.821-1.283)	**0.686*** (.494-.953)	**0.677*** (.487-.941)	0.58 (.326-1.042)
Arthritis or Rheumatism	**1.212**** (1.072-1.370)	1.05 (.905-1.217)	1.104 (.946-1.287)	1.109 (.943-1.305)	1.071 (.894-1.282)	1.177 (.922-1.504)
Cancer	**1.230**** (1.045-1.447)	1.095 (.898-1.336)	0.994 (.748-1.322)	**1.283*** (1.025-1.605)	1.246 (.980-1.586)	1.293 (.956-1.749)
Diabetes	**1.274***** (1.116-1.453)	**1.161*** (.999-1.348)	**1.319**** (1.078-1.615)	0.965 (.791-1.177)	0.893 (.718-1.110)	1.128 (.880-1.446)
High Blood Pressure	**1.161*** (1.030-1.309)	1.055 (.915-1.215)	1.061 (.902-1.248)	1.049 (.874-1.259)	0.992 (.817-1.205)	0.815 (.534-1.243)
Liver Disease	**1.330**** (1.063-1.663)	1.176 (.878-1.575)	Insufficient # Cases	**1.603**** (1.111-2.312)	1.551 (.991-2.427)	Insufficient # Cases
Ulcer GI	**1.151*** (1.013-1.306)	1.097 (.946-1.273)	1.054 (.889-1.250)	1.058 (.868-1.289)	1.028 (.843-1.255)	0.92 (.614-1.377)
Joint Pain (symptom)	**1.141*** (1.018-1.279)	1.053 (.925-1.200)	1.11 (.955-1.289)	1.117 (.963-1.296)	1.073 (.920-1.252)	1.179 (.910-1.527)
Numbness or Tingling (symptom)	**1.128*** (1.008-1.263)	1.092 (.958-1.244)	**1.220*** (1.029-1.446)	1.066 (.915-1.242)	1.04 (.890-1.214)	1.095 (.868-1.381)

laboratory), which reports an upper 95th percentile value of 4 µg/L from 2001-2002.[1,34,35]

PCB Concentrations: Two-hundred and ninety-one volunteers were tested for serum PCB concentrations at NCEH. The mean blood PCB concentration was 2.2 mg/L, with a maximum of 18.6 mg/L. These results were reported in much more congener-specific detail in Schaeffer et al. (2006). Ninety percent of the participants had PCBs values of less than 3.8 mg /L, compared to a 95th percentile value of 2.7 µg/L of the same NHANES age-group.[36]

Potential Confounders to Medical Histories: Age ($r=0.49$, $p<0.001$) was the only confounding variable found to be associated with PCB concentrations, as was expected based upon our earlier work.[30] BMI was highly correlated to Age but not the contaminants and therefore not used as a confounding variable. Age alone was used to construct a model to control for statistically significant relationships between contaminant concentrations and all health conditions.

Other potential confounding variables and general demographic variables were included in all analyses of the associations between PCBs, bHg, and self-reported medical histories. These are reported in Table 4. Medicated shampoo was used by 43 (5%) of respondents and expected to be related to inorganic mercury exposures. Hg speciation using inductively coupled plasma mass spectrometry (ICP-MS) revealed that, on average, only 6% of the total mercury in our samples was from medicated shampoo or other inorganic substances. Significant associations were demonstrated between smoking and heart disease ($p=0.043$) and between alcohol and miscarriages ($p=.036$).

Self-reported Medical History and Contaminants in Fish: Table 3 describes mean fish consumption (g/day) by tribe and the proportion of cases for select health outcomes. The most frequently reported disease histories in which a clinical diagnosis was given by a medical provider were: hypertension (18%), arthritis (18%), allergies (15%), diabetes mellitus (13%), ulcers (11%), miscarriage (10%) and skin disease (10%). Disease history items or medical symptoms which exhibited significant or suggestive associations with the contaminants were: Allergies, Arthritis, Cancer, Diabetes, High Blood Pressure, Liver Disease, Gastrointestinal Ulcers, Joint Pain, and Numbness/Tingling (Table 4). Except for diabetes and allergies, associations between contaminants and health outcomes were lost after accounting for age, though suggestive associations with numbness/tingling reappeared after controlling for age and other confounders.

The relationship between PCBs and diabetes yielded the highest levels of significance (OR = 1.319; $p < 0.014$ after controlling for confounders). Though only suggestive, the relationship between Allergies and bHg showed a lowered risk of adverse health in association with the pollutant. Before controls, allergies were inversely associated with bHg (Odds Ratio=0.69, $p=0.025$) and after controlling for age, allergies still (Odds Ratio=0.68, $p=0.02$) showed a significant inverse association with bHg.

Limitations

The recruitment of the sample population was not random since participants were mostly solicited at tribal health fairs and other community events which are predominantly attended by females. This resulted in a bias towards the female participant (64% of the volunteers). Nevertheless, the self-reported health outcomes match tribal health concerns and priorities.10 Selection bias towards fish consumption concerns was considered minimal since the health fairs topics typically focus on other concerns such chronic illness prevention and social determinants of health. However self-selection for participation in the study was a limitation common to all health fair generated studies which could result in differences not reflected in the tribal populations.

There was a long delay (up to several years) between the collection of samples and the actual chemical analyses at the CDC/NCEH (organochlorines and whole blood mercury). These delays were due to subcontracting and laboratory development issues in Atlanta and beyond the control of the primary OHS research team. All medical histories were self-reported and depended upon the respondent to accurately recall and record past medical conditions (either symptoms or clinical diagnoses). Furthermore, due to the retrospective nature of the study, exposure was assessed after the occurrence of the health outcomes. We are therefore unable to discern between elevated exposures that may have occurred after the health outcome vs before. The contaminant levels are more aptly conceptualized as proximate to the participant's exposure-modifying behaviors.

As an exploratory, post-hoc analysis, the interpretability of the statistical associations between health outcomes and contaminants is limited. Though the analyses may be considered four separate families (one for each contaminant and one for each category of health reporting) a broad adjustment of significance, such as a Bonferroni correction, would only allow us to consider the unadjusted model for PCBs and Diabetes as significant. Finally, all participants were adults. No health outcomes were assessed for the human population thought to be most sensitive to this risk factor: fetuses and neonates. Results should therefore be interpreted in relation to dietary health in adults, not developmental risks.

Discussion

Aside from diabetes, discussed below, this analysis failed to uncover compelling associations between serum contaminants that are related to fish consumption and adult health outcomes. However, interesting and significant patterns were detected between Ojibwe groups, fish consumption, and body burdens of two important fish consumption contaminants. It appears inland tribes consuming walleye and panfish are more susceptible to Hg contamination, whereas tribes who consume lake trout and whitefish from the GL are receiving relatively more exposure from PCBs. This provides important retrospective context when considering fish consumption and future biomonitoring efforts among the tribes. It is interesting to note that, despite perceptions at the time that tribal fish-

dependent diets were leading to increased exposures, contaminants in this population were modest to low and comparable to the general population were observed. At these levels, for adults, it is unsurprising that only suggestive health effects were observed. Whereas the Ojibwe are assumed to consume large amounts of fish, and are therefore more vulnerable to elevated exposures, it appears their vulnerability may lie more in an aversion to traditional dietary food choices. The challenge is to balance traditional food sources, with an aversion to the more contaminated sources, species, and sizes. This highlights the importance of ongoing monitoring in addition epidemiological investigations that can help to estimate the risks and benefits of dietary options to the Ojibwe.

Great Lakes PCB concentrations may be in decline[37] but Hg may increase due to continued proliferation from atmospheric deposition.[34,37] The Centers for Disease Control and Prevention (CDC) National Health and Nutrition Examination Survey (NHANES) study estimated the U.S. mean for total blood mercury in fish eating women to be 1.94 mg /L. Eight percent of these NHANES women had levels greater than the 5.8 mg/L EPA reference dose.[35] The mean level of total blood Hg for women in the Ojibwa Health Study was 1.36 mg /L and only 5 participants (2.6%) were greater than 5.8 mg /L. Hightower and Moore[38] identified high concentrations of mercury in affluent men, women, and children who consumed fish purchased from stores or restaurants, and they reported the mean blood level of Hg in 115 adult patients was 14.0 µg/L, a value well above the 95th percentile in OHS (4.67 µg/L) and still greater than the highest OHS value (11.8 µg/L).[38] These data suggest that the contaminant levels for Ojibwe adults were not uniquely higher than the general public at the time OHS was conducted. However, a key difference between these two groups remains which may yet represent a health disparity: wild-caught fish such as walleye and lake trout are culturally and nutritionally important dietary items to the Ojibwe. Furthermore, in a rural context, where dietary options are limited, fish represent a prominent source of lean protein with high levels of unsaturated fatty acids. Restricting the consumption of certain contaminated fish, as is rightly suggested in governmental consumption advisories, could therefore lead to undesirable health consequences.

Depending on consumption habits, eating traditionally harvested fish in the GL region may not increase overall body burdens of PBT chemicals any more than eating tuna, restaurant, or store bought fish.[39] Other published reports suggest that health conscious people who frequently eat market fish may experience health problems.[38] Furthermore, given new concerns about emerging contaminants such as polybrominated diphenyl ethers (PBDEs) in poultry and red meats, all sources of dietary protein need to be comparably tested and the risks must be communicated in a culturally sensitive manner.[40-42] Intervention strategies for risk communication such as the mercury GIS maps produced by Great Lakes Indian Fish & Wildlife Commission may help guide tribal members to less polluted fish and further reduce adverse health impacts of PBT chemicals,[1] assuming those programs are adequately maintained and updated.

The relationship between metabolic health outcomes and organochlorines/obesogens has become an increasing topic of interest since OHS was conducted.[43,44] In the OHS group, after controlling for age as well as confounders, an increased risk of diabetes was associated with higher levels of PCBs. This relationship persists from the hypothesized link between PCBs and diabetes found in our previous work.[30] Many other studies have suggested this link.[26,27,45-50] Regarding lipids, Schaeffer et al[33] observed that only certain total lipids and serum total triglycerides were correlated only with certain PCB congeners in OHS samples. They further questioned whether or not the relationship between PCBs and serum lipids is coincidental or causal. Some studies suggest that the relationship could be causal, but in the direction of PCBs leading to increased lipids[43,44,51] – as opposed to higher lipids predisposing PCB accumulation. The current analysis is ill-equipped to explore that debate; however, the results reported here support the connection between metabolic disorder and PCBs. This connection should be carefully considered if further biomonitoring efforts are initiated with the Ojibwe.

Working to lower PBT chemicals in fish is essential to encouraging traditional fish diets. The complicated relationship between diabetes (which is of epidemic proportions in most tribes) and organochlorines such as PCBs suggests a need for further investigation. Examining both the benefits and the risks of GL fish consumption is imperative.[52-54] These results highlight the importance of preserving traditional diets through effective risk assessment/communication and by encouraging the continued reduction of contamination for not just Hg and PCBs but all chemicals of health concern in GL food chains. This will only be possible if carefully constructed biomonitoring efforts are embarked upon to service the under-representation of accurate tribal data.

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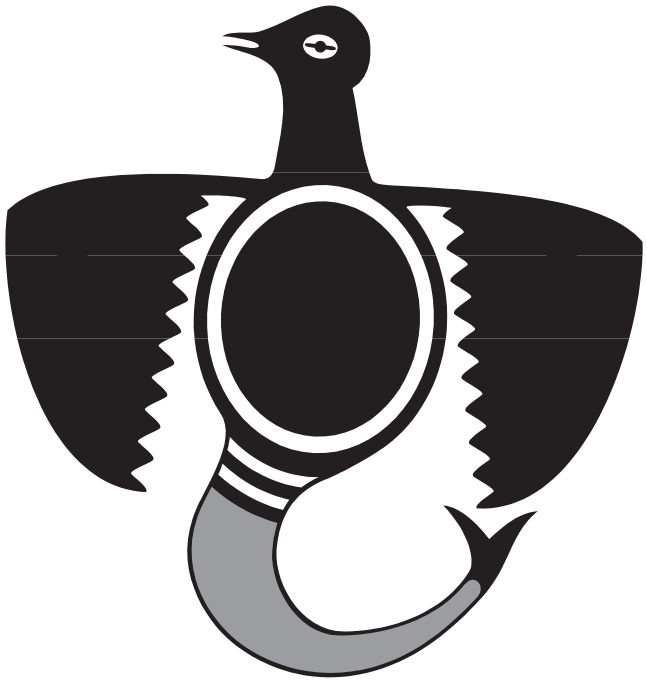


Our Children Are Sacred: A Community Brief on the Health and Wellness of Native American Young Children and their Families in Alameda County

Kurt Schweigman, MPH (Oglala Lakota Tribe)

Introduction

The Native American Community Brief highlights the history, culture, needs and strengths of American Indians and Alaska Natives in Alameda County, California. The purpose and collective goal is to document, share and increase awareness about the Native American community's wellness practices specifically around raising young children and the role that community and family plays. This report can be used to educate providers, policymakers and general public regarding the Native American community, an integral part of Alameda County's diversity.

Who We Are

There are 566 federally recognized American Indian and Alaska Native tribes in the Unites States with 104 in California[1,2]. There are 5.2 million American Indians and Alaska Natives alone or in combination with other race(s) living in America, in California there are 723,225.[3] California is home to more Native Americans than any other state in the Country.[4] According to the 2010 Census there are 26,089 (1.7%) Native Americans residing in Alameda County.[5] The original county indigenous population are the Ohlone Tribe, which are made up of several distinct groups. Their original homelands are from the San Francisco Bay through Monterey Bay and to the lower Salinas Valley6. Alameda County has no federally recognized tribes, the vast majority of Native Americans reside in an urban environment.

Our History

Native American families were being separated from their children at an alarming rate due to public and private agencies placing them with non-Indian families. In response the Indian Child Welfare Act was passed by Congress in 1978. This federal law protects the best interest of Native American children and promote stability and security of tribes and families.[7] In the 1970's, 92% of adopted Native American children in California were placed in non-Native American families, a rate six times greater than any other minority.[8] Much of the county Native American population arrived in the 1950's through 1970's due to the federal mandated Indian Relocation Act. This policy encouraged tribal members from American Indian reservations and rural areas in and outside the state to relocate and assimilate into large urban environments.[9] The San Francisco Bay Area was a major relocation site. Many young children in the county are likely to be third and fourth generation descendants as a result of this policy.

Historical Trauma

Native Americans have experienced Historical Trauma for over 500 years, from enduring physical, emotional, social, and spiritual genocide from American historical and contemporary policies.[10] Federal, regional, and local government policy to eradicate or assimilate Native Americans deeply impacted the health and wellness of families and especially children. Most notable was the federal Indian boarding school system which was implemented in the late 1800's with the philosophy of "killing the Indian to save the man." Native children were forcibly removed from their homes to attend these schools.[10] Because of this intergenerational trauma and other traumas, Native Americans face a myriad of maladies and unhealthy behaviors known as Historical Trauma Response. For example, substance abuse to numb the pain associated with the trauma is a form of Historical Trauma Response.[11] It is clear Native American history is wrought with trauma, many community members continue to bear the emotional scars that reach across generations. However, many Native Americans are seeking out wellness to heal from this suffering through community-defined best practices.[12] Native American children are an important factor in the recovery and wellness of parents.

Economic Disparity

> *"Financial stress and proper shelter are the primary concern for parents over child wellness as their wellbeing becomes secondary if they do not have enough food or other basic needs."*
>
> *— Native American community parent*

In Alameda County 21% of Native Americans live below the poverty level which is three times as much as non-Hispanic Whites (7%).[13] It is important to understand that our Native

American population face economic disparity as well as other hardships within the county. Native American providers and parents within the community have voiced the overwhelming inequality due to low socioeconomic status. The difficulty of low or no employment and other economic challenges for parents add more stress on the wellness of young children.

Racial Misclassification

"When I first moved to Oakland from out-of-state everyone assumed I and my young children were Mexican."

— Native American community parent

Reasons for racial misclassification are complex and vary at health system and individual levels. A provider may fail in collecting Native American identity or assume a different race. Further complications can include stereotyping by having a Spanish surname therefore being classified as Hispanic. Also, some Native Americans may not identify with a particular ethnic or racial identity and may be forced to pick only one race on forms.[14] Ultimately many factors contribute to the under-reporting of Native Americans in health data records and other forms collecting race information. This under reporting can impact needed funding for services specific to Native Americans.

Multiethnic Native Americans

Many Native American families are multiethnic and identify with more than one racial group. Through intermarriage it is not uncommon for Native Americans to have children of multiple ethnicities. Multiethnic parents may identify as Native American and feel strongly about their cultural connection, however they may also feel strongly connected to other ethnicities and racial groups. As Alameda County is mostly urban with a diverse population, Native Americans may experience many cultures and adopt their surroundings when raising their young children.

Native American Culture: What Works

"It is important for my young daughter to learn our tribal traditions… she dances in traditional regalia at Pow Wows, I can see that it makes her happy to have cultural pride."

— Native American community parent

Building a Supportive Community

There was an unexpected consequence from the federal mandated Indian Relocation Act. In the Government attempt to assimilate Native Americans into general society it actually brought Native Americans from different tribes together. In the isolation of relocatees in a large urban environment along with economic difficulty Native Americans sought out each other to build support. Parents gathering at Native American organizations and events help build trust by interacting with other community members with young children. The Intertribal Friendship House in Oakland was established, and for the first time the community had a center for activities. Native American groups and social clubs joined together for a common goal of fostering support to community members.[15] To this day Native American organizations in the county are an integral part of delivering wellness programs to families and children while continuing to build trust among the community.

Spirituality and Wellness

Spirituality is very important to the wellness of family and community. A combination of traditions, traditional spiritual practices, and/or mainstream faiths coexist. Spirituality is usually community-oriented rather than individual-oriented and vary depending upon tribal tradition or western belief.[16] Wellness activities for families and children are wide ranging, some include parenting classes, talking circles, and youth traditional dance practices. Native American community organizations often facilitate and host activities that are based on Native spirituality and wellness. Community organizations bring traditional spiritual healers and cultural healers to the county for healing ceremonies. Faith-based spirituality and churches are also important to many Native American community members.

The Role of Community Events

Native Americans in the densely occupied county are an invisible population, however, community events bring the population together throughout the year. Community events build on the restoration of cultural practices, tribal traditions and values which restore and sustain wellness and balance in families and youth.[12] Native American events in the county include Pow Wows, wellness gatherings, cultural/traditional activities, and other social gatherings. At community events parents often watch and care for each other's children. The role of events and gatherings provide a strong sense of community for Native American families and their young children. It gives opportunity for children to build trusting relationships with the Native American community. Community events create a strong sense of cultural pride and sense of belonging that is important for Native American children and their families.

Health and Wellness of Children

"First and foremost is for children to be in a safe environment, happy, and learning what they need to as they go on the next path of their education."

— Native American childcare provider

What is our vision of a healthy child?

Children are often considered our most important resource in the Native American community. They will carry forward our Native American beliefs, culture and traditions to future generations. There are a myriad of factors that make up a healthy Native American child. Parents often cite healthy children be

energetic, have humor and happiness, be curious about their surroundings and worldview, have normal development physically and behaviorally, and be empathetic. Native parents are also concerned children be in a safe environment where they can thrive. Parents would like to see their children have overall wellness and health to grow and succeed into the future. If children need assistance, their families will often seek out Native American specific organizations they trust.

What role do community members play?

Traditionally in Native American culture it is the tribe/community that help raise children, not just individually by parents. Community members often become extended family, similar to aunts and uncles to children and other youth become cousins. Parents that have experience raising their own young children may notice behaviors of concern and can share knowledge and parenting skills with new parents. This form of community support is important for role modeling and passing along cultural knowledge as well as good parenting advice.

How can providers better serve us?

"[Non-Native American health providers] need to build trust within the community first…without trust from our people, your job would be very difficult."

— Native American childcare provider

Providers unfamiliar with our Native American community should be mindful of not assuming we are all the same. Many Native American families are multicultural and adapt to surrounding culture. However, community members are likely to be strongly identified with Native American traditions and culture. It is often said Native Americans "walk in two worlds" by having both Native American identity and belief as well as being a part of contemporary society. Providers should be aware of contemporary and historical traumas Native American families have endured, which may contribute to the distrust of healthcare systems. It is encouraged that providers make an effort to consult with local cultural advisors for questions.[16] It is important providers understand Native Americans have a strong sense of community built on the restoration (and continuation) of cultural practices, tribal traditions and values that restore wellness and balance to families and youth.[12] It is also important for providers to make efforts to inform community members of available services that can improve their healthcare as well as livelihood (e.g. housing, food banks, etc.).

What are good examples of programs currently in practice?

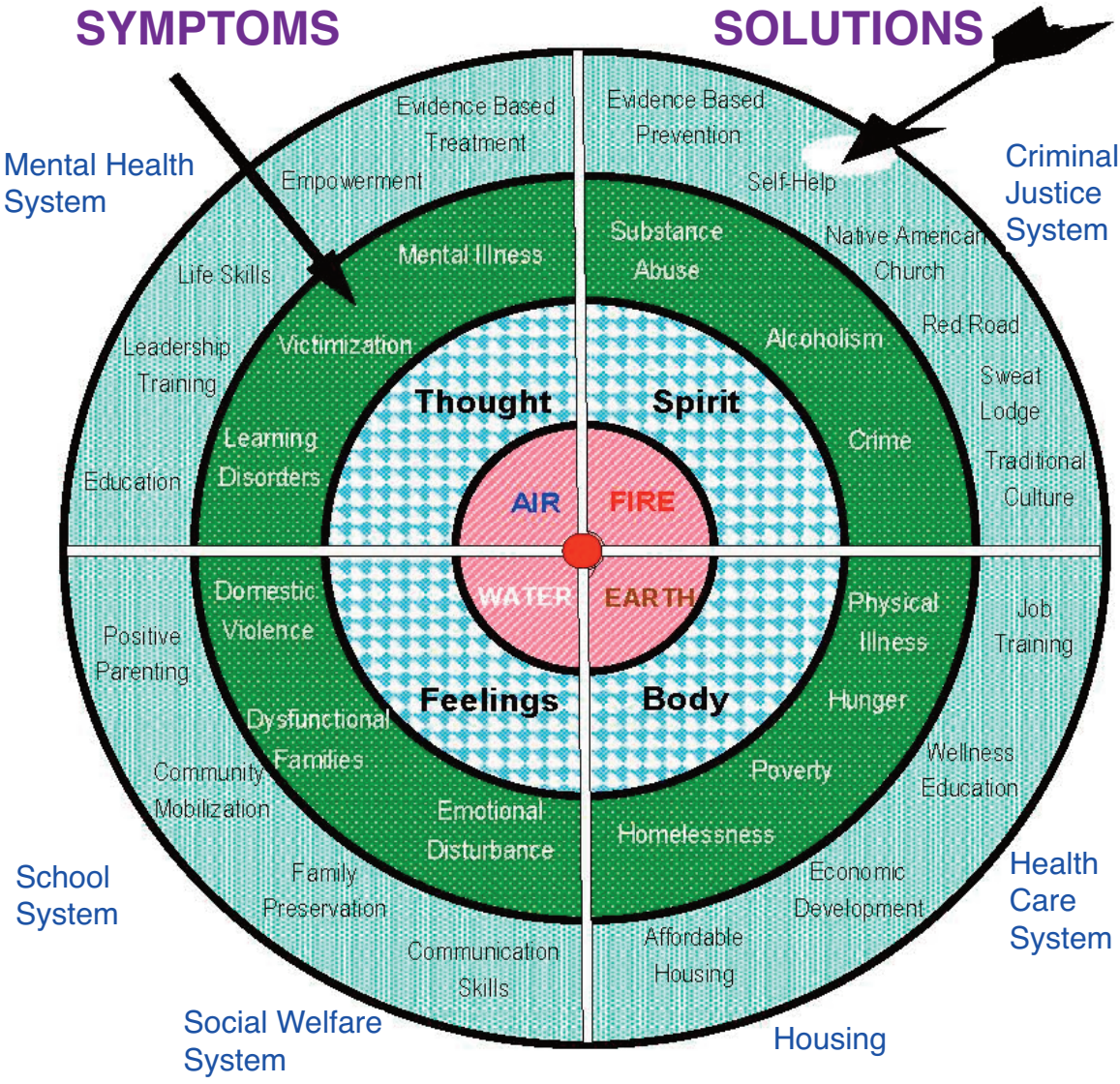
To better understand the Native American community in Alameda County, it is helpful to be familiar with current projects that engage parents and their young children aged 0 to 5. The Strong Family Home Visiting project at the Native American Health Center in Oakland is a home visiting program that provides services to pregnant and parenting families with Native children under the age of three. The project utilizes the evidence-based Family Spirit Program that is culturally-tailored for providers and parents for wellness of physical, cognitive, social-emotional, language learning and self-help of pre-school aged children.[17] The Fatherhood Is Sacred program offers classes at the Intertribal Friendship House in Oakland. The program strengthens families by responsibly involving Native fathers in their lives of their children.[18] It is important for Native fathers to be "present" in the lives of their children as well as teach their children culture, language, and traditional values.[19] Positive Indian Parenting is a nationally accepted curriculum for parents that provides a structured format to develop and incorporate traditional Native American practices and values into modern-day childrearing.[7] Although there are only three programs mentioned here, there are others in practice that address directly or in-directly the health and wellness of young children within the county. Most programs targeting Native American families and children are contingent upon funding with defined timelines.

Holistic System of Care for Native Americans in an Urban Environment

The best evidence of success for the system of care model for the Native American population are programs that utilize services that embody a unique blend of western and indigenous traditions.[20] Providers to Native American young children in Alameda County need to understand community wellness is linked across generations from young children to elders. It is also linked at the treatment and prevention levels. The model contains several principles including support for advocacy efforts of parent groups and the well-being of young children. The Holistic Model was developed by the Community Wellness Department (CWD) at the Native American Health Center and adopted by the Native American community in the San Francisco Bay Area.[21] CWD provides outpatient mental health and substance abuse counseling for Native Americans in San Francisco and Oakland. Services include individual, group and family/youth counseling, positive parenting, cultural activities, and Native American specific traditional healing. The Holistic Model focuses on solutions rather than problems. (Figure 1) The inner circle shows the basic elements and core value of indigenous belief followed by symptoms and solutions.[22]

With the welfare of young children strongly taken into account in the Holistic Model, family members are actively involved in all aspects of planning, carrying out, and evaluating the system of care and individualized care plans.[22] The Holistic Model allows supportive resources for child care, improved provider-family communication, educating providers about the history and structure of Native American culture, and integration of western and Native American traditional healing. In a Holistic Model ten-year perspective CWD found a decrease of aggressive behavior, depressive and anxious feelings in severely emotionally disturbed Native American children.[23]

Figure 1. Holistic System of Care for Native Americans in an Urban Environment[22]



Community Organizations Offering Wellness

"Support can come in the form of organizations that our community members trust."

— Native American community parent

It is important for providers, policymakers, and community members to know about Native American organizations within the county that provide health and wellness services to Native American families and their young children. The American Indian Child Resource Center *www.aicrc.org* offers youth and family support services that provide culturally appropriate activities and programs. Services include cultural arts for youth and Foster Care home certification and assistance. Hintil Kuu Ca, (510) 531-8400, is a Native American childcare program that enhances academic skills and incorporates American Indian culture and values. Established in 1955 the Intertribal Friendship House, *www.ifhurbanrez.org*, is the Native American community cultural center that also offers social services. They offer culture and traditions through hosting Pow Wows, drumming and traditional dance practice, native language classes, and many other ceremonial and social gatherings. The Native American Health Center, www.nativehealth.org, offers culturally-based holistic care with out-patient medical, dental, and behavioral wellness services. They also offer youth services and community based wellness events. Their media center creates digital stories of local Native American community

members *www.nativehealth.org/gallery/video/view/93*. All of the above-mentioned Native American agencies are located in the City of Oakland.

In conclusion, it is the intention of this community brief to serve as a general information guide of the Native American population with regard to the health and wellness of our young children and their parents living in Alameda County. The author would like to especially thank the four Native American community members in Alameda County that took part in key-informant interviews. The author would also like to acknowledge First 5 Alameda for making this report possible. It is our hope this information will be useful to educate and inform about our Native American community. For more information about First 5 Alameda visit their website *www.first5alameda.org* or contact Ann Chun, Cultural Access Services Administrator at 510-227-6948.

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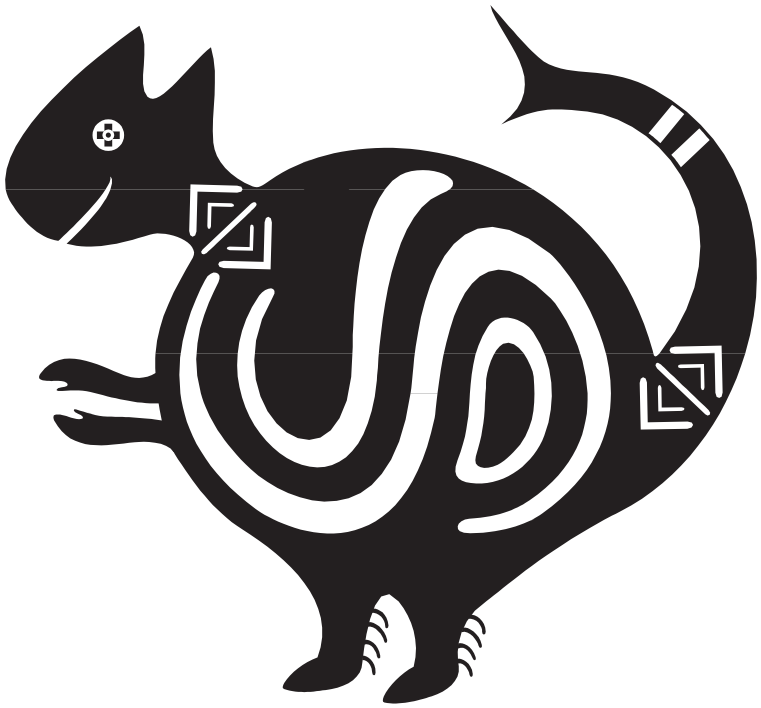

Indian Health Service
National Pharmacy and Therapeutics Committee
Calcium Channel Alpha-2-Delta Ligands
Use in Neuropathic Pain Management
NPTC Formulary Brief
May 2014

Background:

The IHS National Pharmacy and Therapeutics Committee (NPTC) reviewed the calcium channel alpha-2-delta ligands, gabapentin and pregabalin, and their place in the treatment of neuropathic pain at the May 2014 meeting. The NPTC last reviewed treatment of diabetic neuropathy in September 2010 and added gabapentin to the National Core Formulary based on evidence available at that time. Neuropathic pain is defined as pain resulting from a disturbance of the central or peripheral nervous system. The general prevalence of neuropathic pain is reported as 2 to 18%. Painful diabetic neuropathy (PDN) and postherpetic neuralgia (PHN) have prevalence rates of about 15%. Both gabapentin and pregabalin are FDA approved for treatment of PHN. Pregabalin is also FDA approved for treatment of diabetes associated and spinal cord injury associated neuropathic pain as well as for fibromyalgia. Gabapentin is not FDA approved for treatment of neuropathic pain; however, it is commonly used in the treatment of various types of neuropathic pain.

Discussion:

Publications from the British National Institute for Clinical Excellence (NICE), Cochrane Review Committee, the OHSU Drug Effectiveness Review Project, the Canadian Pain Society, the International Association for the Study of Pain, and the European Federation of Neurological Sciences were reviewed.

Gabapentin and pregabalin were both shown to be effective in the treatment of neuropathic pain. A majority of the reviews looked specifically at diabetic neuropathy and post-herpetic neuralgia. In all of the guidelines, gabapentin and pregabalin, in addition to antidepressant (discussed separately), were recommended as first line agents in the treatment of neuropathic pain with the exception of trigeminal neuralgia. There was no preference as to which agent should be tried first. If one first line agent was ineffective, it was recommended to try a different first line agent.

Gabapentin exhibits nonlinear pharmacokinetics and as its dose is increased, bioavailability decreases and less drug is absorbed. It should be titrated up from a low starting dose until either analgesia is achieved or side effects experienced. Maximum recommended doses are 3600mg/day for PDN and 1800mg/day for PHN. Efficacy may be seen in as little as 2 weeks, but may take several months for an adequate therapeutic trial. Pregabalin has linear pharmacokinetics and requires a shorter titration period. It is not effective for PDN at a dose of 150mg/day. The maximum recommended dose of pregabalin is 300mg/day for PDN and 600mg/day for PHN. Both agents must be dose adjusted for renal insufficiency.

Data suggests that only between 1 in 10 and 1 in 4 will get > 50% pain reduction with these agents. It is important for patients to be educated that these agents do not eliminate pain, but help to make it manageable and improve quality of life. Withdrawal of these agents secondary to adverse events was 11% for gabapentin and 18-28% for those taking pregabalin.

There is a need for more studies looking at the calcium channel alpha-2-delta ligands and their use in the many different types of neuropathic pain. Use of these agents in combination with other treatment options for neuropathic pain is an area that is lacking strong recommendations.

Findings:

The NPTC decided to take no action in regards to changing the National Core Formulary. This decision was primarily based on the lack of data recommending one of the calcium channel alpha-2-delta ligands over the other. Pregabalin is still under patent and significantly more costly than gabapentin. Pregabalin is a controlled substance which requires more inventory control than gabapentin. Thus, gabapentin remains on the NCF and pregabalin has not been added at this time.

If you have any questions regarding this document, please contact the NPTC at IHSNPTC1@ihs.gov. For more information about the NPTC, please visit the NPTC website.

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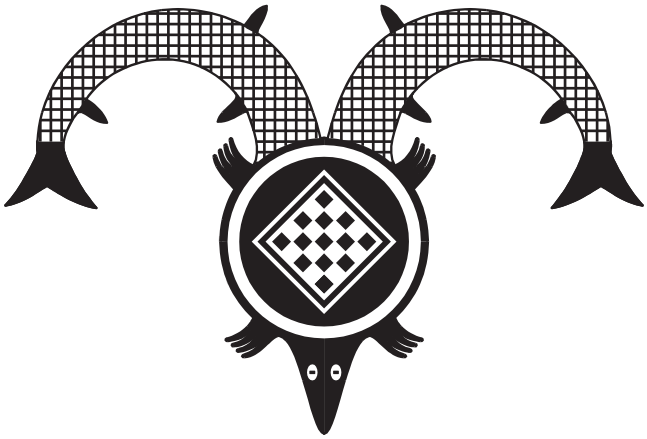

Indian Health Service
National Pharmacy and Therapeutics Committee
Skeletal Muscle Relaxants
NPTC Formulary Brief
May 2014

Background:

In May 2014, the IHS National Pharmacy and Therapeutics Committee (NPTC) evaluated current guidelines and recommendations for the use of skeletal muscle relaxants (SMRs). Evaluation criteria included published evidence on the pharmacology, pharmacodynamics, pharmacokinetics, safety, efficacy, utilization and procurement data of the SMRs: baclofen, carisoprodol, cyclobenzaprine, methocarbamol and tizanidine. Carisoprodol is the only federally controlled substance in this class due to its wide potential for abuse.[5] SMRs are a heterogeneous group of centrally acting medications used to treat spasticity from upper motor neuron syndromes and muscular pain or spasms from peripheral musculoskeletal conditions.[3] SMRs work directly on the contractile mechanism of the skeletal musculature or through transmission in spinal cord motor reflex pathways.[3] They act to produce decreased muscle tone and involuntary movement with minimal loss of voluntary motor function and/or consciousness.[3]

Discussion:

The guideline from the American Pain Society and the American College of Physicians for acute low back pain recommends first-line treatments of acetaminophen and non-steroidal anti-inflammatory drugs (NSAIDS).[8] The guideline recommended to reserve SMRs as an alternative treatment. According to the Clinical Guideline from Chou et al (2007), Medications for Acute and Chronic Low Back Pain (1292 abstracts), the most common medications prescribed are: NSAIDS, SMRs and opioid analgesics. There is good evidence for the short-term effectiveness of SMRs for acute (<4 weeks duration) low back pain. Evidence is insufficient to identify one medication as being overall advantageous due to the complex trade-offs between benefits and harm.[2] SMRs alone had a total of 36 trials reviewed (all 2 weeks or less in duration) for spasticity and musculoskeletal conditions and one high quality Cochrane review for acute low back pain.[2] In these reviews, tizanidine was shown to be efficacious for low back pain, but has increased adverse events (ADE's).[2] Evidence from the Cochrane review identified tizanidine plus APAP or NSAID is consistently better than APAP/NSAIDs alone for short-term pain relief.[2] Practitioners should consider risk factors for complications, concomitant medication use, baseline severity of pain, duration of low back pain symptoms and cost before adding SMRs to first line pain therapy.[2] Tizanidine and baclofen are indicated for the treatment of muscle spasticity and carisoprodol, cyclobenzaprine and methocarbamol are indicated for the treatment of musculoskeletal disorders.

A Cochrane Review evaluating muscle relaxants for non-specific low back pain analyzed 30 trials (23 high quality) and indicated strong evidence that any of the SMR's are more effective than placebo alone and are similar in performance, yet adverse events are more prevalent and require caution with use.[9] Also, further trials are needed to compare SMRs to other analgesics and NSAIDS.[9] Three high-quality trials (560 patients) showed that tizanidine plus analgesics were more effective in providing pain relief and decreasing muscle spasm than analgesics alone.[8,9] Several reviews consistently confirm that SMRs are associated with increased adverse drug events (ADE), even with short-term use.[6,8,9] The most common ADEs are dizziness and drowsiness.[6] However, data is low-quality and limited in quantity.[6]

Comparative Efficacy and Safety of SMRs for Spasticity and Musculoskeletal Conditions: A Systematic Review, published in the Journal of Pain and Symptom Management Review, was comprised of 101 randomized trials and 98 reports including: systematic reviews, meta-analyses, head-to head trials, and placebo-controlled trials.[3] Comparative efficacy of SMRs utilized for spasticity showed no pattern to suggest one SMR was better than others, but a possible increased efficacy of tizanidine.[3] Efficacy for musculoskeletal conditions showed that cyclobenzaprine was associated with better 'global improvement' scores.[3] Comparative safety of SMRs utilized for spasticity showed increased adverse events, no associated deaths, and abuse was not evaluated.[3]

Tizanidine showed an asymptomatic increase in LFTs.[3] Data for musculoskeletal conditions showed cyclobenzaprine

caused more somnolence vs methocarbamol.[3] Overall results showed tizanidine was effective for both spasticity and musculoskeletal conditions.[3] Spasticity (primarily in multiple sclerosis) showed baclofen and tizanidine had similar effectiveness and rates of ADEs vs. placebo.[3] Cyclobenzaprine, carisoprodol and tizanidine are effective vs. placebo.[3] Safety and efficacy for many SMRs was not determined with this data.[3]

See and Ginzburg (2008) recommendations for low back and neck pain include short-term relief with the moderately effective carisoprodol, cyclobenzaprine, or tizanidine.[8] Cyclobenzaprine is the most heavily studied SMR with consistently proven effectiveness.[3,8] Cyclobenzaprine with naproxen showed greater decrease of spasm and tenderness.[8] The authors concluded, SMRs place in therapy is debatable as they are not considered first-line therapy, but rather adjunctive short-term therapy for musculoskeletal conditions or acute low back pain.[8] Evidence does not clearly support any one SMR medication. Specific selection should be based on side-effect profile, patient preference, abuse potential, drug interaction potential, and any other special characteristics of the SMR.[8] Effectiveness data is limited and toxicity data is strong. Cyclobenzaprine was useful for low back pain or fibromyalgia.[8] Methocarbamol was found useful if the sedation from cyclobenzaprine or tizanidine was unwanted.[8] Carisoprodol is metabolized into meprobamate and should be used as a last-line because of its abuse potential.[5,8] Standardized high-quality evidence and current primary literature for this class of medications is limited.

Findings:

A wide variety of pain conditions, both acute and chronic, may be accompanied by painful muscle spasm. SMRs can be useful in treating this aspect of the patient's symptoms, but their action may be more the result of sedation rather than muscle relaxation. These medications may also cause CNS depression and should be used cautiously when combined with other CNS depressant medications. SMRs are primarily used as adjunctive medication for pain relief due to spasticity or musculoskeletal conditions. There is some clinical merit for utilizing SMRs based on appropriate patient-specific conditions. Based on the information presented, the committee made no changes to the IHS National Core Formulary (NCF) and did not add a SMR to the NCF. However, these agents may be appropriate for inclusion on local formularies to meet the needs of the patient population. Carisoprodol should be avoided due to its abuse potential. The NPTC will continue to monitor SMR medications for future consideration.

If you have any questions regarding this document, please contact the NPTC at *IHSNPTC1@ihs.gov*. For more information about the NPTC, please visit the NPTC website.

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MEETINGS OF INTEREST

Advancements in Diabetes Seminars
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Join us monthly for a series of one-hour WebEx seminars for health care program professionals who work with patients who have diabetes or are at risk for diabetes. Presented by experts in the field, these seminars will discuss what's new, update your knowledge and skills, and describe practical tools you can use to improve the care for people with diabetes. No registration is necessary. The accredited sponsors are the IHS Clinical Support Center and IHS Nutrition and Dietetics Training Program.

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EHR is the Indian Health Service's Electronic Health Record software that is based on the Resource and Patient Management System (RPMS) clinical information system. For more information about any of these courses described below, please visit the EHR website at *http://www.ihs.gov/CIO/EHR/index.cfm?module=rpms_ehr_training*. To see registration information for any of these courses, go to *http://www.ihs.gov/Cio/RPMS/index.cfm?module=Training&option=index*.

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POSITION VACANCIES

Editor's note: As a service to our readers, The IHS Provider will publish notices of clinical positions available. Indian health program employers should send brief announcements as attachments by e-mail to the.provider@ihs.gov. Please include an e-mail address in the item so that there is a contact for the announcement. If there is more than one position, please combine them into one announcement per location. Submissions will be run for four months and then will be dropped, without notification,, but may be renewed as many times as necessary. Tribal organizations that have taken their tribal "shares" of the CSC budget will need to reimburse CSC for the expense of this service ($100 for four months). The Indian Health Service assumes no responsibility for the accuracy of the information in such announcements.

Psychiatrist
Zuni Comprehensive Community Health Center;
Zuni, New Mexico

The Zuni Comprehensive Community Health Center (Indian Health Service) has an opening for a full-time psychiatrist to see adults and children. We do psychotherapy, crisis work, trauma work, as well as work with families, couples, and groups. You will have the opportunity to impact and design mental health for the community as a whole. We are shielded from managed care. You have an opportunity to provide psychotherapy to your patients and families without worrying about insurance approvals. You are not merely hired as a prescriber, but as a biopsychosocial psychiatrist. In this job, you have a chance to feel good about the care you are providing, in a setting that is personally and professionally stimulating, and in a place where your skills are needed and valued. Additional advantages include market pay, no call, and excellent federal benefits.

We are located on the Zuni reservation. The Zuni Pueblo is one of the oldest continuously inhabited Native American villages in the US, estimated to be at least 800-900 years old. The Zuni are located on their ancestral lands and have one of the most intact Native American cultures in the country. Zuni tradition and the Zuni language are a living and vibrant part of daily life in the community. Zuni is nestled amongst beautiful red rock mesas and canyons. It is considered high desert at 6000 - 7000 feet and is located in the northwestern region of New Mexico, along the Arizona border.

For more information or to apply, contact Michelle Sanchez, Zuni Service Unit Behavioral Health; telephone (505) 782-7312; e-mail *michelle.sanchez2@ihs.gov*. (3/14)

Staff Clinician
Department of Health and Human Services,
National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases,
Division of Intramural Research
Phoenix, Arizona

The Diabetes Epidemiology and Clinical Research Section (DECRS), Phoenix Epidemiology and Clinical Research Branch (PECRB), National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) conducts research in the epidemiology and prevention of type 2 diabetes, its complications, and related conditions, primarily among American Indians in the southwestern United States. The section is recruiting a staff clinician to take part in clinical research activities. The position is located in Phoenix, Arizona on the campus of the Phoenix Indian Medical Center.

The staff clinician will work in an interdisciplinary, collaborative environment and have the following responsibilities: a) medical director of the DECRS research clinics, supervising nurse practitioners and medical assistants, and overseeing clinic schedules and operations; b) principal or associate investigator of randomized clinical trials in prevention of diabetes or its complications; c) principal or associate investigator of epidemiologic investigations of type 2 diabetes and related conditions; and d) associate investigator in a randomized clinical trial of optimizing weight gain in pregnancy and effects on the mother and child. There are outstanding opportunities to collaborate with experts in epidemiology, clinical research, physiology, genetics, and biostatistics. Ample clinical, laboratory, and computing resources are available.

The position requires licensure to practice medicine in one of the United States or D.C. and board eligibility or certification, preferably in internal medicine, pediatrics, family practice, or preventive medicine. Clinical or epidemiological research training and experience are desirable. Salary and benefits will be commensurate with experience and qualifications. Outside candidates and current federal employees (civilian or commissioned corps) are encouraged to apply.

Interested candidates may contact William C. Knowler, MD, DrPH, Chief, DECRS, c/o Ms. Charlene Gishie. To apply, please send a cover letter; CV with publications list; and names and contacts of three references to Ms. Charlene Gishie, National Institutes of Health, 1550 E. Indian School Rd, Phoenix, AZ 85014; e-mail *charlene.gishie@nih.gov*. The deadline to submit an application is March 7, 2014.

NIDDK is a component of the National Institutes of Health (NIH) and the Department of Health and Human Services (DHHS). All positions are subject to a background

investigation. DHHS and NIH are Equal Opportunity Employers. (1/14)

Family Practice Physicians (2)
Cass Lake IHS Hospital; Cass Lake, Minnesota

Leech Lake Reservation is an open reservation located in Minnesota's Northwoods region. Towering pines fringe many of the lakes found within its boundaries. Wild rice beds, deep forests, and shimmering lakes, two of which are among the largest in the state, abound. There are approximately 1,050 square miles within the reservation, nearly all of which is within the boundaries of the Chippewa National Forest.

When you locate here, you are looking for a quality of life for both your workers and your family. That is why it will be worth your while to find out how much Leech Lake can offer with its natural beauty, friendly communities, good schools, and various civic, cultural, and historical organizations. The area also provides many quality outdoor recreational activities, from fishing and boating in the summer to nordic and alpine skiing in the winter. Though Leech Lake's natural beauty, civic attractions, and recreational activities are things to behold, they pale in comparison to the friendliness of the people of the Leech Lake area.

The population within the reservation boundaries is estimated at 91,800. Nearly fifty-eight percent are between the ages of 16 and 65. The resident American Indian population on the reservation has been estimated at 7,763 by the census. Most of the population is concentrated in eight communities dispersed across the reservation. Adjacent to the reservation, there are three major area economic centers: Bemidji, which is 13 miles to the west of Cass Lake; Grand Rapids, which lays 54 miles to the east of Cass Lake; and Walker, roughly 23 miles to the south of Cass Lake.

The Cass Lake Indian Hospital is owned and operated by the Federal Government as a Public Health Service, Indian Health Service Facility. We have a staff of 120 employees, six of whom are physicians and five nurse practitioners; there is a contracted emergency department service. Additional services include ambulatory clinic, dental, optometry, audiology, laboratory, radiology, physical therapy, and diabetes clinic. Our Facility has 13 beds; we had 223 discharges and 1,398 patient days in FY '05. According to the most recent data, we have 99,503 outpatient visits annually, 5,612 Dental visits, and 2,763 Optometry visits; there are 20,512 registered patients. The Leech Lake Tribe operates mental health, substance abuse, podiatry, and diabetes clinics, as well as seven other clinics staffed by various professionals.

For additional information, contact Antonio Gruimaraes, MD, Clinical Director (family medicine at telephone (218) 335-3200; e-mail *antonio.guimaraes@ihs.gov*, or Tony Buckanaga, Physician Recruiter, at telephone (218) 444-0486; e-mail *tony.buckanaga@ihs.gov*. (1/14)

THE IHS PRIMARY CARE PROVIDER
A journal for health professionals working with American Indians and Alaska Natives

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