

Is lead a concern in Canadian autistic children?

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BACKGROUND: The Centers for Disease Control and Prevention (CDC) threshold for intervention for blood lead level (BLL) is greater than 0.48 µmol/L, but new research suggests that there are adverse effects at any level of exposure. Children with autism are at increased risk for lead exposure and intoxication, and have later and more prolonged exposures because of exploratory oral behaviours and pica.

OBJECTIVE: To estimate the mean BLL and prevalence of high BLL in a convenience sample of autistic children living in northern Alberta, based on the CDC threshold for intervention.

METHODS: Children with autism were recruited from the clinics at the Glenrose Rehabilitation Hospital in Edmonton, Alberta. A complete blood count and differential, serum ferritin and BLL were requested after consent was obtained. Summary statistics were reported. For dichotomous outcomes, proportions were presented. Continuous outcomes for the two groups with a BLL of 0.1 µmol/L or greater, or less than 0.1 µmol/L were compared.

RESULTS: None of the children tested had a BLL exceeding 0.48 µmol/L. Nine children (19%) had BLLs of 0.1 µmol/L or greater but less than 0.48 µmol/L, and 39 (81%) had BLLs of less than 0.1 µmol/L. Those with a BLL of 0.1 µmol/L or greater had significantly more pica or oral exploratory behaviours.

CONCLUSION: Children with autism in northern Alberta may not be at risk for elevated BLLs that exceed the CDC threshold for intervention. They should be screened for lead exposure risk factors and tested if there are risks, especially behaviours relating to pica and oral exploration of objects. Clinicians may need to further explore the reasons for low-level exposures to lead in the autistic population.

Key Words: Autism; Development; Environment; Lead; Toxins

Lead is an environmental toxin whose health risk effects on the developing nervous system have been studied over time (1-3). Adverse behavioural effects have been documented even at very low levels of lead, and recent studies (2,3) have confirmed that there does not seem to be a threshold for the effects of lead on the developing child, with impacts on IQ, attention, learning and social-behavioural conduct. The Centers for Disease Control and Prevention (CDC) has progressively lowered the level of concern for blood lead levels (BLLs) over time from 1.45 µmol/L in 1975 to 0.48 µmol/L in 1991 (4), where it currently stands as a result of new knowledge of

Doit-on s'inquiéter des taux de plomb chez les enfants autistes canadiens?

HISTORIQUE : Les Centers for Disease Control and Prevention (CDC) préconisent d'intervenir lorsque le taux de plomb dans le sang (TPS) dépasse un seuil de 0,48 µmol/L, mais d'après de nouvelles recherches, tout taux d'exposition s'associerait à des réactions indésirables. Les enfants autistes sont plus vulnérables à une exposition et à une intoxication au plomb et y sont exposés plus tard et pendant une période plus prolongée en raison de leurs comportements oraux exploratoires et de leur pica.

OBJECTIF : Évaluer le TPS moyen et la prévalence de TPS élevé dans un échantillonnage de commodité d'enfants autistes qui habitent dans le nord de l'Alberta, d'après le seuil d'intervention des CDC.

MÉTHODOLOGIE : Les auteurs ont recruté des enfants autistes dans les cliniques du Glenrose Rehabilitation Hospital d'Edmonton, en Alberta. Ils ont obtenu leur formule sanguine et leucocytaire, leur ferritine sérique et leur TPS après avoir reçu les autorisations nécessaires. Ils ont déclaré un résumé des statistiques. En cas de dichotomie des résultats, ils présentaient plutôt des proportions. Ils ont comparé les résultats continus des deux groupes pour qui le TPS équivalait à au moins 0,1 µmol/L ou était inférieur à 0,1 µmol/L.

RÉSULTATS : Aucun des enfants à l'étude ne présentait un TPS supérieur à 0,48 µmol/L. Neuf enfants (19 %) avaient un TPS d'au moins 0,1 µmol/L mais inférieur à 0,48 µmol/L, et 39 (81 %) un TPS inférieur à 0,1 µmol/L. Ceux dont le TPS était d'au moins 0,1 µmol/L faisaient beaucoup plus de pica ou avaient des comportements exploratoires beaucoup plus marqués.

CONCLUSION : Les enfants autistes du nord de l'Alberta ne sont peut-être pas vulnérables à des TPS élevés dépassant le seuil d'intervention des CDC. Ils devraient subir un dépistage pour connaître leurs facteurs de risque d'exposition au plomb et subir des tests s'ils y sont vulnérables, surtout s'ils ont des comportements liés au pica et à l'exploration orale des objets. Les cliniciens devraient peut-être explorer davantage les raisons de la faible exposition au plomb au sein de la population autiste.

the adverse neurodevelopmental and health effects. The CDC acknowledges that new research since 1991 provides evidence of adverse effects at lead levels below 0.48 µmol/L (1,4,5). Canfield et al (2) showed blood lead concentrations below 0.48 µmol/L are inversely associated with IQ scores at three to five years of age and associated declines in IQ are greater at these concentrations than at higher concentrations.

Autism is a neurobehavioural disorder characterized by disturbances in reciprocal social interactions, social communication and repetitive, stereotypical behaviours (6). Children with autism often have pica – the habitual

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ingestion of nonfood items – and habitual mouthing of objects (7). These behaviours extend much longer than the usual pattern seen in other populations and may place children with autism at a disproportionately higher risk for lead exposure than normal children (7-10). There is very little research on the prevalence of lead intoxication in children with autism. A literature search produced only eight articles that specifically addressed lead exposure in this population (7-14). Cohen et al (10) found a significantly higher level of blood lead in an autistic group of children than in their normal siblings. In 1982, Cohen et al (9) screened 33 children with autism (mean age of 18.2 years) and found BLLs between 0.24 $\mu\text{mol/L}$ and 2.61 $\mu\text{mol/L}$ (mean $0.91 \pm 0.55 \mu\text{mol/L}$).

Shannon and Graef (8) reviewed the charts of 17 lead-poisoned children with pervasive developmental disorders (PDDs), including autism, and compared them with 30 lead-poisoned children without PDD. They found that lead intoxication among children with PDD may appear de novo beyond the third year of life, and may be associated with a high rate of re-exposure in spite of environmental prevention measures.

The purpose of the present study was to estimate the mean BLL and prevalence of high BLL in a convenience sample of autistic children living in northern Alberta, based on the CDC threshold for intervention.

METHODS

Children were recruited from the Glenrose Rehabilitation Hospital Preschool Assessment Service (PAS) and Autism Follow-up Clinic (AFC). PAS is a specialty clinic that provides a multidisciplinary team assessment and diagnosis for children in northern Alberta up to six years of age who are referred with complex developmental concerns. The team includes a licensed psychologist, speech and language therapist, occupational therapist, developmental paediatrician and social workers. The AFC is a follow-up clinic for children up to the age of 18 years in northern Alberta who have had a multiteam assessment and *Diagnostic and Statistical Manual of Mental Disorders* (fourth edition) diagnosis of autism spectrum disorder (including autism, Asperger's syndrome and PDD-not otherwise specified). The team has licensed paediatricians, child psychiatrists, psychologists, speech and language therapists, occupational therapists, social workers and dietitians available.

Ethics board approval was obtained before the onset of the study. A letter of invitation to participate in the study, along with a general information package, was given to families who received the diagnosis of autism spectrum disorder at their PAS team assessment. Invitations were also extended to the families attending the AFC. An informed consent form was signed by each recruited parent or guardian, and information on the study objectives and protocol were made available.

Children were included if they had a multiteam assessment and diagnosis of autism spectrum disorder, were between the ages of three and 10 years inclusive, were living

in northern Alberta at the time of the study, and had completed the bloodwork requested. Sixty-seven families gave consent to be a part of the study during the recruitment period from July 1, 2005, to June 30, 2008. Eight children were excluded because they were outside the stated age range, and 12 children were excluded because they did not follow through with the blood tests requested after giving consent. A total of 48 children were included in the study.

Data on the age, sex, the area of residence (urban being those living in Edmonton, Alberta, and rural being those living outside of Edmonton), and behaviours that may place children at risk, such as pica or oral exploration of objects, were collected for each child. A complete blood count and differential, serum ferritin and blood lead were requested from each participant, and a number assignment was given for the purpose of group analysis. Information on individual patient identification was held confidential. Blood lead tests were analyzed using the PerkinElmer Elan 6100 Inductively Coupled Plasma Mass Spectrometer by a method called inductively coupled plasma mass spectrometry. This method meets the standard set by the College of Physicians and Surgeons of Alberta, and the College of American Pathologists. As well, external proficiency testing is routinely performed to ensure that the range of standards of BLL is consistent across laboratories. Our current external proficiency testing is performed with the Wisconsin State Laboratory of Hygiene. This program replaced the CDC program in the late 1980s.

For ease of comparison across studies, all blood lead concentration units have been converted to $\mu\text{mol/L}$. To convert $\mu\text{mol/L}$ to $\mu\text{g/dL}$, multiply by 20.72; $0.483 \mu\text{mol/L} = 10 \mu\text{g/dL}$. The cut-off values for ferritin (less than 10.0 $\mu\text{g/L}$ for children aged three to five years and less than 12 $\mu\text{g/L}$ for children aged six to 11 years) were used as an indicator of iron deficiency, which is at the fifth percentile for age (National Health and Nutrition Examination Survey [NHANES]) (15,16). Because the values for low ferritin vary among centres (6 $\mu\text{g/L}$ to 22 $\mu\text{g/L}$), a value of greater than 12 $\mu\text{g/L}$ but less than 22 $\mu\text{g/L}$ was also recorded as a range for 'at risk' of iron deficiency. Hemoglobin (Hb) and mean corpuscular volume (MCV) were recorded as g/L and fL, respectively. The cut-off for Hb of less than 110 g/L for children aged two to four years and less than 120 g/L for children aged five to 10 years, and MCV less than 80 fL were used as measures of iron-deficient erythropoiesis (15-17). Summary statistics were reported as mean \pm SD and medians with ranges. For dichotomous outcomes (eg, "BLL exceeding or not the level of $0.48 \mu\text{mol/L}$ "), proportions were presented. Characteristics were presented for the group as a whole as well as separate for those with high and low lead levels. The characteristics of the latter two groups were compared statistically. Continuous outcomes were compared using an unpaired *t* test, while dichotomous outcomes were compared using Fisher's exact test. Those identified with abnormalities of complete blood count or serum ferritin were offered appropriate management or referred to their attending physician at their request. Children with BLLs of 0.1 $\mu\text{mol/L}$ or greater

TABLE 1
Summary of bloodwork findings of 48 Canadian autistic children

Outcome	n	Mean \pm SD	Median (range)
Age, years	48	5.4 \pm 2.1	5.0 (3.0–10.8)
Blood lead, μ mol/L	48	0.082 \pm 0.082	0.05 (0.02–0.42)
Hemoglobin, g/L	42	130.94 \pm 8.3	131.5 (111–150)
MCV, fL	42	82.2 \pm 4.5	83 (61–88)
Ferritin, μ g/L	40	29.8 \pm 17.7	25 (7–86)

MCV Mean corpuscular volume

were offered a referral to the Pediatric Environmental Health Specialty Unit in Edmonton for further exposure assessment and management.

RESULTS

Results were obtained on 14 female (29%) and 34 male (71%) autistic children, with 35 (71%) from urban and 13 (27%) from rural environments in northern Alberta (Table 1). None of the children had BLLs exceeding the current threshold for intervention (greater than 0.48 μ mol/L) set by the CDC (1). Nine children (19%) had BLLs greater than or equal to 0.1 μ mol/L but less than 0.48 μ mol/L, and 39 children (81%) had BLLs less than 0.1 μ mol/L. Table 2 provides details of the blood results and behaviours of the nine autistic children with BLLs of 0.1 μ mol/L or greater.

Of the entire group of children, 23 (48%) had pica, 27 (56%) had oral exploratory behaviours, and 31 (65%) had pica and/or oral exploration behaviours identified. The group was divided into those with BLLs at or above 0.1 μ mol/L and those with levels below 0.1 μ mol/L. All the variables were combined and compared between the two groups. The group with BLLs at or above 0.1 μ mol/L had significantly higher behaviours of pica or oral exploration of objects (Table 3). All nine children with BLLs at or above 0.1 μ mol/L had behaviours of pica and/or oral exploration of their environment.

Estimates of iron deficiency and iron deficiency anemia based on data collected from the NHANES survey of 1988 to 1994 (15) indicate that 3% of children three to five years of age and 2% of children six to 11 years of age were iron deficient using the cut-off values for ferritin as less than 10.0 μ g/L for children three to five years of age and less than 12 μ g/L for children six to 11 years of age, which is at the fifth percentile for age (NHANES). Of those who had ferritin measured (40 of 48 children), one child (9%) between six and 10 years of age and two children (5%) between three and 5.9 years of age had levels below the cut-off level in keeping with the reported prevalence rates of iron deficiency for those age ranges (15–17). If one uses the cut-off for ferritin as less than 22 μ g/L, then 17 of the 40 children (42.5%) may have or may be at risk for iron deficiency. Only one child had Hb less than cut-off for age, and this was not associated with a low MCV, a low ferritin or BLL greater than 0.1 μ mol/L. Five children (12.5%) had MCV less than 80 fL not associated with low Hb, but two of these children had BLL at 0.1 μ mol/L. None of the variables, including Hb, MCV or ferritin, were significantly related to the BLLs in the present study (Table 3).

TABLE 2
Results of nine autistic children with blood lead level 0.1 μ mol/L or greater

Age	Hb, g/L	MCV, fL	Ferritin, μ g/L	Blood lead, μ mol/L	Pica or oral exploration	Region (urban or rural)
4 years, 1 month	134	84	39	0.18	yes	urban
4 years, 3 months	137	80	26	0.28	yes	urban
6 years	–	–	47	0.26	yes	rural
4 years, 1 month	134	82	17	0.18	yes	urban
3 years, 1 month	122	79	38	0.1	yes	rural
10 years, 3 months	133	88	10	0.11	yes	urban
8 years, 6 months	134	84	21	0.32	yes	urban
6 years	134	84	–	0.1	yes	urban
10 years	130	74	30	0.42	yes	rural

Hb Hemoglobin; MCV Mean corpuscular volume

TABLE 3
Differences in mean patient characteristics by high and low lead levels

Outcome	High lead level (\geq 0.1 μ mol/L)	Low lead level (<0.1 μ mol/L)	Difference or OR (95% CI)	P
Number of patients	9	38		
Age, years	6.25 \pm 2.71	5.22 \pm 1.86	1.03 (–0.88–2.95)	0.18
Hemoglobin, g/L	132.3 \pm 4.56	130.5 \pm 9.02	1.72 (–2.50–5.94)	0.61
MCV, fL	81.9 \pm 4.22	82.3 \pm 4.58	–0.42 (–3.61–2.77)	0.81
Ferritin, μ g/L	28.5 \pm 12.4	30.7 \pm 19.0	–2.18 (–12.52–8.17)	0.76
Proportion with pica	9/9 (100)	24/39 (61.5)	∞ (1.03– ∞)	0.041
Proportion in rural area	3/9 (33.3)	9/39 (23.1)	1.67 (0.22–9.82)	0.67

For continuous outcomes, values are presented as mean \pm SD. For dichotomous outcomes, values are proportions with percentages. P values are computed with unpaired t tests for continuous outcomes and with Fisher's exact test for dichotomous outcomes. MCV Mean corpuscular volume

DISCUSSION

Because information on lead exposure has been unavailable for autistic children in Alberta, the results of our study represent new baseline information. None of the autistic children studied had BLLs exceeding the threshold for intervention (greater than 0.48 μ mol/L) set by the CDC. The fact that nine (19%) had BLLs of 0.1 μ mol/L or greater but less than 0.48 μ mol/L remains a concern, because it has been shown that there are adverse effects on cognitive development even at lower levels. It is not known whether these mildly elevated rates of BLL compare with the general Canadian paediatric population or with other paediatric populations in Alberta because of the lack of broader-based

TABLE 4
Summary of Canadian regional lead surveys after 1990

Author, year (reference)	Date of survey	Site	Population	Geometric mean BLL (µmol/L)	BLL ≥0.48 µmol/L
Rhains and Levallois, 1993 (21)	1990	Quebec City, Quebec	Umbilical cord blood, n=823	0.094 (95% CI 0.099–0.099)	<1%
Kosatsky and Boivin, 1994 (28)	1990	Montreal, Quebec	6 months to 5 years, n=52	0.27 (95% CI 0.22–0.33) (range 0.11–1.01)	5.80%
Koren et al, 1990 (20)	1990	Toronto, Ontario	Umbilical cord blood, n=95	0.08±0.07	0%
Goulet et al, 1996 (30)	1991	St Jean-sur-Richelieu, Quebec	0–10 years, n=75	0.24 (95% CI 0.22–0.27)	0%>0.72 µmol/L
Balram, 1993 (31)	1991	St John, New Brunswick	1–3 years, n=97	0.23	–
Gagné, 1994 (32)	1991	Rouyn-Noranda, Quebec	2–5 years, n=87	0.35 (95% CI 0.85; GSD 0.074)	33%
Langlois et al, 1996 (33)	1992	South Riverdale, Ontario	0–6 years	0.189	–
Smith and Rea, 1995 (19)	1992	Moose Factory, Ontario, and Moosonee, Ontario	1–6 years, n=395	0.15 (95% CI 0.14–0.05) (range 0–0.91)	4%
Smargiassi et al, 2002 (29)	1992–1995	Montreal, Quebec	Umbilical cord blood, n=160	0.082±0.082 (5th–95th percentile 0.039–1.88)	4.30%
Rhains et al, 1999 (22)	1993–1995	Southern Quebec	Umbilical cord blood, n=1109	0.076 (95% CI 0.074–0.079) (range 0.01–3.10)	0.16%
Levesque et al, 2003 (24)	1993–1996	Nunavik, Quebec	Umbilical cord blood, n=475	0.19 (95% CI 0.18–0.20)	6.90%
Willows and Gray-Donald, 2002 (25)	1998–2000	Northern Quebec	9-month-old Cree, n=186	median 0.08 (range 0.01–1.00) (25th–75th percentile 0.05–0.12)	2.70%
Lorenzana et al and Hiltz, 2003 (26,27)	1991 1992 1993 1994 1995 1996 1997 1998 1999	Trail, British Columbia	6–60 months	0.65 0.57 0.55 0.58 0.46 0.53 0.42 0.39 0.29	–
Hiltz, 2003 (27)	2001	Trail, British Columbia	6–36 months	0.23	–
Hanning et al, 2003 (23)	2002	Mushkegowuk Territory, Ontario	Umbilical cord blood, n=91; at 4 months, n=85	0.10±0.08; 0.08±0.05	3%

Values are presented as mean ± SD unless otherwise specified. BLL Blood lead level; GSD Geometric standard deviation

Canadian prevalence studies. Most of the lead studies in Canada were regional surveys of children exposed to point sources of lead pollution (5) (Table 4).

The majority (65%) of the group studied had pica and/or oral exploration of objects at a mean age of 5.4 years, which is much older than the age one would expect these behaviours (7). A high rate of pica in the autistic population is supported by previous research in which 60% were found to have had pica at some stage (7). Our results suggest that pica and oral exploration of objects may place children with autism at risk for exposure to environmental lead. The mild elevations of BLL in those with pica and oral exploration of objects may also suggest that the environment where these children live is, at least, relatively free of environmental lead.

We do not have an overall representative picture of current BLLs in Canadian children, but an approximation can be derived from previous studies performed on specific populations (5,18–29) (Table 4). The last national blood survey was conducted in 1978, but this was before lead was removed from gasoline. Regional surveys performed in the

past 15 years reveal that most Canadian children have BLLs below 0.48 µmol/L, with elevated levels between 2% and 11% of the populations studied (Table 4). In general, BLLs of children living near industry in Canada have declined over time partly because of industrial emission controls and soil remediation, but the greatest influence has been the overall reduction of lead in the environment (1,5). These efforts are partly offset by consumer products marketed toward children (1,8). Although there is no recent lead surveillance in Canadian children, the United States surveillance data show a steep decline in BLL from the 1976 to 1980 period to the 1991 to 1994 period mainly because of lead removal from gasoline and food cans (4). Certain United States groups remain at risk, ie, non-Hispanic black race, families with lower income and those living in older housing built before 1946 (4). Furthermore, studies (6–14) have shown that children with developmental disorders are at risk, particularly those with autism.

The CDC and American Academy of Pediatrics recommend that preventive care for every child should include obtaining an environmental history and identifying

occupational lead exposures among household members (3,4). Regular child care visits should include screening questions that identify children at risk, but more importantly, provide preventive anticipatory guidance to all parents about lead poisoning in their children (3). Most of the practice parameters for the screening and diagnosis of autism recommend lead screening be restricted to those with identifiable risk factors for excessive lead exposure, specifically those with pica (15-17). Current guidelines do not include children with autism as a group requiring special consideration in defining the child at high risk for lead intoxication, yet research has shown that oral sensory seeking and pica behaviours are prevalent and do not always diminish around four years of age as in other developmentally delayed children, making them vulnerable in environments normally considered safe for children (21-26). This vulnerability to environmental lead exposure remains high in autistic children in spite of the provision of standard hazard reduction measures (22). It is important for professionals to consider regular lead monitoring for populations at higher risk, and they should have a high index of suspicion when assessing children with developmental delays (1,3), especially those with pica and oral exploratory behaviours.

Although public health initiatives to remove environmental sources of lead have been very effective, low-level exposures are ubiquitous, their effects are not easily recognized and our understanding of the effects of these low-level exposures is only in its infancy (1). Identified sources of lead exposure in Canadian children include consumer products directed at children and house dust/soil close to point industrial sources (1,2). The task of identifying and limiting exposures among Canadian children is therefore possible and should be undertaken in those found with levels below current regulatory standards. Clinicians are more likely to investigate low levels if regulatory standards are aligned with scientific knowledge of harmful effects.

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CONCLUSION

Autistic children in northern Alberta may not be at risk for elevated BLLs that exceed current CDC guidelines. However, 19% of the group studied had results above the new level of concern (greater than 0.1 µmol/L). Children with autism should be screened for lead exposure risk factors and tested if there are risks, especially behaviours relating to pica and oral exploration of objects. Clinicians need to be aware of the health impacts of BLLs below current regulatory standards, and be prepared to identify those at risk and assess for sources of exposure. Clinicians may be more likely to investigate low BLLs if regulatory standards are aligned with scientific knowledge of harmful effects. Broad-based Canadian screening studies on the prevalence of lead and other toxins in children are necessary to provide primary care workers with much needed information on the groups within our population who are at higher risk for toxin exposures.

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