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Assessment of Human Health Risks of Consumption of Cadmium Contaminated Cultured Oysters

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ABSTRACT

With farmed British Columbia (BC) oysters containing higher cadmium concentrations than wild oysters, long-term exposure to cadmium through consumption of oysters has the potential to cause health risks. This study reports on a risk assessment for cadmium intake resulting from the consumption of BC-cultured oyster. The study concludes that Health Canada's current recommended BC-cultured oyster consumption rate for Canadians of 12 oysters per month exceeds the Agency for Toxic Substances and Disease Registry chronic oral minimal risk levels (MRL) of 0.2 $\mu g \cdot kg^{-1} \cdot day^{-1}$ by approximately 4- to 5-fold and reaches the Food and Agriculture Organization/World Health Organization (FAP/WHO) reference dose of 1 $\mu g \cdot kg^{-1} \cdot day^{-1}$ for cadmium consumption for Canadians. This suggests that although the current recommended maximum oyster consumption rates is consistent with the FAO/WHO and U.S. Environmental Protection Agency limits for acceptable risk, it leaves little or no room for error or uncertainty. This is noteworthy as recent studies demonstrate toxicological effects at cadmium intakes of 0.43 to 0.71 $\mu gCd \cdot kg^{-1} \cdot day^{-1}$. This study indicates that a lower maximum BC-cultured oyster rate should be considered, particularly for high risk groups, including women with low iron stores, people with renal impairment, smokers, children, and indigenous people who consume organ meats of games and wildlife other than shellfish.

Key Words: cadmium, oyster, human health, risk, hazard.

INTRODUCTION

British Columbia (BC) oyster production is a multimillion-dollar industry with great economic potential (Web citation 1). The leading areas of oyster production in BC are Cortez Island, Desolation Sound, Baynes Sound, and the Sunshine Coast (Web citation 2). In years 1999 to 2000 shipments of oysters from British Columbia

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were turned back from Hong Kong market, because they exceeded limits on cadmium for imported shellfish. Import limits are 3–4 $\mu g \cdot g^{-1}$ in the U.S., 2 $\mu g \cdot g^{-1}$ in Hong Kong and Australia, and 1 $\mu g \cdot g^{-1}$ in New Zealand (Broten 1998; Kruzynski 2002). Canada has no import standard for cadmium in oysters.

There are no historical data on cadmium concentrations in farmed oysters on the BC West Coast prior to 2000 (Kruzynski 2002). The Canadian Food Inspection Agency (CFIA) tested cadmium concentration in BC-cultured oysters in 2000 and found the average cadmium concentration was 2.63 $\mu g \cdot g^{-1}$ wet weight (shucked meat) (Kruzynski 2002). The highest concentrations reached 4.56 μg $Cd.g^{-1}$ in 2-year old oysters (Kruzynski 2002). A market survey of cadmium concentrations in farmed oysters purchased from various seafood outlets in the lower mainland of Vancouver reported concentrations ranging from 0.9 to 3 $\mu g \cdot g^{-1}$ wet weight (Brunjes and Bendell-Young 2005, unpublished data). In comparison, the Canadian Total Diet Study (1993–1999) lists fresh or frozen shellfish to contain 0.0153 $\mu g \cdot g^{-1}$ wet weight, *i.e.*, much lower than cadmium concentrations in BC-cultured oysters. Cultured oysters were reported to contain higher levels of cadmium than wild oysters (Kruzynski 2000) and other shellfish (Kruzynski 2002). Inter-tidal or wild oysters feed during high tides only. Current aquaculture practices result in oysters being continuously submerged and therefore feeding 24 h a day, unlike inter-tidal oysters that do not feed between tides. The longer feeding period may be one of the causes for high cadmium content in cultured oysters.

The Joint Food and Agriculture Organization and World Health Organization (FAO/WHO) Expert Committee on Food Additives (JECFA) established in its 16th meeting a Provisional Tolerable Weekly Intake (PTWI) for cadmium of 400 to 500 μg of cadmium per adult person. This corresponds to a provisional tolerable cadmium intake of 0.81 (*i.e.*, 400 ÷ 7 ÷ 70) to 1.01 $\mu g \cdot kg^{-1} \cdot day^{-1}$, which was simplified to 1 $\mu g \cdot kg^{-1} \cdot day^{-1}$ and left unchanged in subsequent meetings (JECFA 2004). However, Cd-linked bone and kidney toxicities were observed in people whose dietary Cd intakes were well within the PTWI (Satarug and Moore 2004). Exposure levels of 30 to 50 μg Cd per day for adults or 0.43 to 0.57 $\mu g \cdot kg^{-1} \cdot day^{-1}$ have been associated with increased risk of bone fracture, cancer, kidney dysfunction, and hypertension (Satarug *et al.* 2000; Satarug *et al.* 2003). It is therefore possible that the FAO/WHO weekly suggested limit is under-protective and that consumers are at risk while their cadmium intake is below the PTWI.

The Canadian Guidelines for dietary intake of cadmium through oyster consumptions advise a limit of oyster consumption of 12 oysters a month for adults (*i.e.*, 3 $person^{-1}$ $week^{-1}$). Ignoring cadmium intake from other dietary sources, intake of three BC farmed oysters (average weight ranges from 40 to 50 g) high in cadmium produces an intake ranging between 315 μg per week (*i.e.*, 3 $week^{-1}$ × 40 g × 2.63 $\mu g \cdot g^{-1}$) and 395 μg per week (*i.e.*, 3 $week^{-1}$ × 50 g × 2.63 $\mu g \cdot g^{-1}$) or between 0.64 and 0.80 $\mu g \cdot kg^{-1} \cdot day^{-1}$. This is less than the JECFA's PTWI for 70 kg adults of 490 μg per week (or 1 $\mu g \cdot kg^{-1} \cdot day^{-1}$) but above the Agency for Toxic Substances and Disease Registry (ATSDR) chronic oral minimal risk levels (MRL) of 0.2 μg kg^{-1} day^{-1} (ATSDR 1999) and within the range of exposures (*i.e.*, 0.43 to 0.57 $\mu g \cdot kg^{-1} \cdot day^{-1}$) associated with human health effects. The Canadian Environmental Protection Act Assessment Report for Cadmium and its Compounds (CEPA 1994) states that members of the general population in Canada are exposed to

cadmium compounds in amounts that are at or near those that have been associated with mild effects on the kidney. The WHO reaffirmed during the 16th, 33rd, and 41st meetings that "there is only a relatively small safety margin between exposure in the normal diet and exposure that produces deleterious effects" (Web citation 3). It is therefore possible that cadmium in Pacific oysters may contribute to potential health concerns.

The objective of the present work is to explore the human health risk associated with Cd intake by consuming BC-cultured Pacific oyster (*Crassostrea gigas*) and to make recommendations with regards to oyster consumption.

METHODS

This study applies the National Academy of Science risk assessment paradigm (NRC 1983) for human health risk characterization. The risk assessment comprises of hazard identification, dose-response (effects) assessment, exposure assessment and risk characterization. Human exposure from each exposure route was calculated according to (USEPA 1998; Han *et al.* 1998), *i.e.*,

$$TDI_i = (\Sigma CE_i \cdot EF \cdot ED)/(BW \cdot AT), \quad (1)$$

where TDI is the total daily intake of cadmium ($\mu g \cdot kg^{-1} \cdot day^{-1}$), ΣCE is the chemical exposure from all sources (including dietary, soil, water, and/or oysters, and/or tobacco smoke (μg person^{-1} · day^{-1}), EF is the exposure frequency (365 days · year^{-1}), ED is the exposure duration (70 years), BW is the body weight (70 kg) and, AT is the averaging time for exposure duration (ED × 365 days.year^{-1} = 25,550 days).

Hazard quotients (HQ) for each exposure route i were determined as

$$HQ_i = TDI_i/R_fD \quad (2)$$

following the U.S. Environmental Protection Agency (USEPA) Region III Risk-Based Concentration Table, January–June 1996 (USEPA 1996), where, R_fD is the oral reference dose ($\mu g \cdot kg^{-1} \cdot day^{-1}$). The recommended FAO/WHO reference dose (R_fD) of 1 μg Cd.kg^{-1}·day^{-1} for a 70 kg man is used. The USEPA reference dose is also 1 μg Cd.kg^{-1}·day^{-1}, based on a NOAEL (no observed adverse effects level) of 10 μg Cd.kg^{-1}·day^{-1} and an uncertainty factor of 0.1. The Hazard Index (HI) was then derived as $\sum HQ_i$.

To assess toxicity of cadmium, we examined studies that delineate health problems at different exposures. Only non-cancer health effects were examined in the present work.

RESULTS AND DISCUSSION

Hazard Identification

Animals can absorb and bioaccumulate cadmium from the environment (WHO 1992; Satarug *et al.* 2003). Some shellfish have high accumulation rates of cadmium and can accumulate up to 120 $\mu g \cdot g^{-1}$ wet weight without apparent ill effect (Kruzynski 2002). Mussels can accumulate up to 1000 μg Cd · g^{-1} without effects on

growth (Fischer 1988). Oysters are able to concentrate cadmium above the maximum permissible limits for edible consumption (Rosas *et al.* 1983). According to the Codex Alimentarius Commission standards, Maximum Permissible Concentration (MPC) for Cadmium in most foods ranges between 0.05 $\mu g \cdot g^{-1}$ and 1.0 $\mu g \cdot g^{-1}$ (such as in mollusks) (Web citation 4).

The main sources of human exposure to cadmium are air, water, soil, food, and cigarettes. Cadmium levels in urban air are typically in the range of 2 to15 $ng \cdot m^{-3}$ (Elinder 1985; WHO 1992; OECD 1994). These levels are higher than those found in rural areas (0.1 to 5 $ng \cdot m^{-3}$), but are lower than those found near active lead or zinc smelters (300–700 $ng \cdot m^{-3}$) (Bernard and Lauwerys 1986; Hutton 1983). In Canada, the mean concentration of Cadmium in drinking water from various studies is 0.044 $\mu g \cdot L^{-1}$ (Dabeka *et al.* 1987). The current USEPA maximum contaminant level (MCL) and Canadian guidelines for cadmium in drinking water are 5 $\mu g \cdot L^{-1}$ (USEPA 1991; EBI Web citation 5). A typical soil concentration of cadmium is 0.06 to 1.1 $\mu g \cdot g^{-1}$ (Web citation 6). Cadmium is a non-essential element in human nutrition. For Canadians, the primary routes of exposure to cadmium are through food and tobacco use. Foods containing the highest cadmium concentrations include meat organs (142 $ng \cdot g^{-1}$), peanut butter and potato chips (86 and 100 $ng \cdot g^{-1}$), cabbage and raspberries (84 and 93 $ng \cdot g^{-1}$), and cooking fats and salad oils (90 $ng \cdot g^{-1}$) (Canadian Total Diet Study 1993–1999). Fresh or frozen shellfish contain 15.3 ng $Cd.g^{-1}$ (Web citation 7).

The two main storage sites for cadmium in the human body are the liver and the kidney. For low-level exposures in the general environment, about 30–50% of the cadmium body burden is stored in the kidneys, with concentrations in the cortex being approximately 1.25 times higher than in the kidney as a whole. Absorbed cadmium accumulates mainly in the renal cortex and liver (JECFA 2004). In non-occupationally exposed subjects the concentration of cadmium in the liver increases with age. Cadmium is eliminated from the organism mainly via urine. The amount of cadmium excreted daily in urine is, however, very small. It represents only about 0.005–0.01% of the total body burden per day, corresponding to a biological half-life of about 18 to 33 years (Kjellstrom 1992). Antagonists of cadmium, Cu, Fe, and Zn, tend to decrease cadmium uptake (McLaughlin *et al.* 1999).

Exposure Assessment for Canadians

Exposure assessment is based on Canada's 1994 *Assessment Report for Cadmium and its Compounds*: (1) Respiration: The maximum intake from air for adults 20 to 70 years old is estimated at 0.09 $\mu g \cdot person^{-1} \cdot day^{-1}$. Based on U.S. data, urban dwellers may inhale between 0.1 to 0.7 $\mu g \cdot day^{-1}$ (Friberg *et al.* 1974). (2) Water Consumption: The exposure from consumption of drinking water per day is approximately 0.036 $\mu g \cdot person^{-1} \cdot day^{-1}$ for 20 to 70 years-old adults. (3) Soil Ingestion: The estimated maximum cadmium intake of the 20 to 70 years old from soil is 0.023 $\mu g \cdot person^{-1} \cdot day^{-1}$. Environmental exposure to cadmium (air, dust, and water) does not contribute significantly to background exposure except in the immediate vicinity of a smelting operation (Friberg, 1974). (4) Dietary Uptake: Data from the U.S. Food and Drug Administration (FDA) Total Diet Study (TDS, 7-year summary, 4/82–2/89) (E. Gunderson, FDA, Division of Contaminants Chemistry, unpublished data)

suggest that the mean lifetime exposure to total cadmium from all food (excluding shellfish) is approximately 10 $\mu g \cdot person^{-1} \cdot day^{-1}$. This value is also reported in the JECFA assessment (2004). A Canadian group examined dietary intake of cadmium in their study of 24 individuals in 5 cities (Dabeka *et al.* 1987) and found that the cadmium intake averaged 13.8 $\mu g \cdot person^{-1} \cdot day^{-1}$ (Dabeka *et al.* 1987), *i.e.*, comparable to the FDA's TDS results. A dietary study including 110 individuals conducted by Dutch researchers found an average daily cadmium intake of 10 $\mu g \cdot person^{-1} \cdot day^{-1}$ (Ellen and Van Loon 1990). Based on the typical cadmium content of relevant foods, Satarug *et al.* (2000 and 2003) reported the highest cadmium intake of 29.3 $\mu g \cdot person^{-1} \cdot day^{-1}$ for Australians not including shellfish consumption as a route of exposure.

Cadmium concentrations in country foods from kidneys and livers of moose, caribou, and deer ranged between 0 and 1,869 $\mu g \cdot g^{-1}$ wet weight, with the highest concentrations found in moose kidney (Kim *et al.* 1998). Cadmium concentrations in traditional food groups were comparable with those of Canadian market food. Highest levels of cadmium were found in the liver and kidney of caribou and moose. Cadmium intakes from traditional food estimated by dietary recall ranged from 0.01 to 1713 $\mu g \cdot person^{-1} \cdot day^{-1}$ (Kim *et al.* 1998). Average cadmium intakes for women and men from traditional food were estimated to be 9% and 6%, respectively, of the FAO/WHO Provisional Tolerable Intake. Kim *et al.* 1998 showed that approximately 20% of indigenous people may consume caribou and/or moose liver or kidney 1 to 5 times per week in winter and summer. Receveur *et al.* (1998) reported that both male and female of northern indigenous people at 40 to 60 years age group consume a daily intake of 112 g of moose liver. This suggests that cadmium dietary intakes in certain sections of the population can reach values as high as 30,000 to 150,000 $\mu g \cdot person^{-1} \cdot day^{-1}$ over certain periods in their lives, *i.e.*, far above the provisional tolerable intake of 70 $\mu g \cdot person^{-1} \cdot day^{-1}$. The potential effect of cadmium intake on this sub-population raises concerns and requires further study.

The average cadmium concentration in BC oysters is 2.63 $\mu g \cdot g^{-1}$ for 40–50 g oysters (Kruzynski 2002). This implies a cadmium uptake rate of 42 to 53 $\mu g \cdot person^{-1} \cdot day^{-1}$ based on the Health Canada maximum recommended consumption rate of 12 oysters per month, *i.e.*, approaching the FAO/WHO established PTDI for cadmium of 70 $\mu g \cdot person^{-1} \cdot day^{-1}$ for dietary intake from all sources.

Because one cigarette contains 0.5 to 2 μg of cadmium, of which 10 to 20% may be inhaled (Nordberg 1974; Elinder 1985), people smoking 20 cigarettes per day can therefore be exposed to 2 to 4 μg Cd.$person^{-1} \cdot day^{-1}$ (Elinder *et al.* 1983; Web citation 8). Similarly, based on Canada's 1994 *Assessment Report for Cadmium and its Compounds*, estimated cadmium intake for cigarette smokers is 3.7 $\mu g \cdot person^{-1} \cdot day^{-1}$ for adults 20 to 70 years old**.** Direct measurement of cadmium concentrations in body tissues confirms that smoking doubles the cadmium body burden above levels observed in individuals not smoking (ATSDR 1999). The latter study suggests that the combined cadmium exposure may be as high as 20 $\mu g \cdot person^{-1} \cdot day^{-1}$ in smokers, compared to approximately 10 $\mu g \cdot person^{-1} \cdot day^{-1}$ in non-smokers (Elinder *et al.* 1976; Hallanbeck 1984). The average cadmium inhaled from cigarette smoking was 2.31 ± 1.00 $\mu g \cdot person^{-1} \cdot day^{-1}$ (Kim *et al.* 1998). The total cadmium intake via market and traditional food and cigarette smoking was estimated to be 137 μg per week (Kim *et al.* 1998).

The combined uptake rate of cadmium in non-indigenous Canadians can therefore be estimated at approximately $0.09 + 0.036 + 0.023 + 13.8$ or $14.0\ \mu g \cdot person^{-1} \cdot day^{-1}$ in non-smokers and approximately $14 + 3.7 = 17.7\ \mu g \cdot person^{-1} \cdot day^{-1}$ in smokers not consuming cultured BC oysters. The uptake rate can be expected to be substantially higher in indigenous Canadians who consume certain country foods. Consumption of cultured BC oysters at Health Canada's maximum recommended rate of 12 oysters per month would raise the estimate of the cadmium uptake rate to approximately 59 to 70 $\mu g \cdot person^{-1} \cdot day^{-1}$ in non-smokers and 63 to 74 $\mu g \cdot person^{-1} \cdot day^{-1}$ in smokers. These estimates are very close or at the FAO/WHO tolerable daily intake of 70 μg Cd person^{-1} day^{-1}. The background exposures estimated here are mean values for people not living near point sources of cadmium contamination. The background exposures estimated for those living or working near high concentration sources of the contaminants will need to be evaluated using information specific to those sites.

Toxicity Assessment

Nephrotoxicity from cadmium exposure increases prevalence of low molecular-weight proteinuria (Nogawa *et al.* 1992; Olsson *et al.* 2002). Renal tubular dysfunction and consequent proteinuria are generally accepted as the main effects following long-term, low-level exposure to cadmium. An estimate of the risk for the development of nephrotoxicity in humans as a result of long-term exposure to cadmium can be obtained from epidemiological observations of the occurrence of tubular proteinuria among workers occupationally exposed to airborne cadmium for long periods of time (Nordberg 1993). Another method of estimating the risk of development of nephrotoxicity from cadmium exposure is to use model calculations based on information on the chemobiokinetics of cadmium and on the critical concentration of cadmium in the renal cortex. Such model calculations indicate that exposure to a cadmium concentration of 14 $\mu g \cdot m^{-3}$ in industrial air during the workdays of the year for 25 years would give rise to an accumulation of cadmium in the renal cortex of 200 $\mu g \cdot kg^{-1}$. This concentration corresponds to an approximate 10% excess risk of low molecular-weight proteinuria (Nordberg 1993). In long-term low-level exposure, cadmium accumulates in the kidney and gives rise to renal tubular damage (Nordberg 1993).

Long-term renal tubular dysfunction may lead to abnormalities of calcium metabolism. Both human and animal studies indicate that skeletal damage (osteoporosis) may be a critical effect of cadmium exposure (Jarup *et al.* 1998b). A characteristic feature of chronic cadmium poisoning, as seen in a cadmium-contaminated area in Japan, was osteoporosis and osteomalacia (Kjellstrom 1992; Tsuchiya 1992). It was termed the itai-itai ("ouch-ouch") disease. Symptoms of this disease include weak bones that lead to deformities, especially of the spine, or to more easily broken bones. It is often fatal (Schroeder 1974). Further, cadmium may damage the testes (male reproductive glands) and may affect the female reproductive cycle (Web citation 9) at significantly higher doses than are the focus of the present work.

Experimental studies have suggested that low-dose exposure to cadmium may affect life cycle related diseases and reproductive toxicity including endocrine disrupting effects (Kaji *et al.* 2002). However, epidemiological studies did not clearly

support the experimental observations. Further research is required to determine whether cadmium is responsible for the aggravation of life cycle related diseases or has the capability to act as an environmental endocrine disrupter in humans (Kaji *et al.* 2002).

On the basis of a multicompartmental model (Kjellstrom and Nordberg 1978; Nordberg and Kjellstrom 1979) for cadmium distribution in the body and the estimated deviation of cadmium levels in the renal cortices of human populations, it has been estimated that a daily cadmium intake of 55 $\mu g \cdot day^{-1}$ in food (population average) would lead to 0.1% of the population reaching the "critical" cadmium concentration of 200 $\mu g\ g^{-1}$ wet weight in the renal cortex after 50 years and develop tubular proteinuria (Kjellstrom *et al.* 1984; Piscator 1985; WHO 1989). For concentrations of cadmium in renal cortex not to exceed 50 $\mu g \cdot g^{-1}$, total intake should not exceed approximately 1 $\mu g \cdot kg^{-1} \cdot day^{-1}$ continuously for 50 years (this assumes an absorption rate of 5%, and that 10% of the absorbed daily dose is rapidly excreted, and a daily excretion of 0.005% of the body burden). The PTDI for cadmium was therefore set at 70 $\mu g \cdot person^{-1} \cdot day^{-1}$ (*i.e.*, 70 $kg \cdot person^{-1} \times 1\ \mu g \cdot kg^{-1} \cdot day^{-1}$) and the WHO/FAO established a reference dose (R_fD) for cadmium of 1 $\mu g \cdot kg^{-1} \cdot day^{-1}$ (JECFA 2004), which is equivalent to 57 $\mu g \cdot person^{-1} \cdot day^{-1}$ for a 70 kg person. The USEPA reference dose for cadmium is also 1 $\mu g \cdot kg^{-1} \cdot day^{-1}$, based on a NOAEL (no observed adverse effects level) of 10 $\mu g \cdot kg^{-1} \cdot day^{-1}$ and an uncertainty factor of 0.1. However, more recent studies indicate that exposure levels of 30 to 50 μg cadmium per day for adults (or 0.43 to 0.71 $\mu g \cdot kg^{-1} \cdot day^{-1}$) are associated with increased risk of bone fracture, cancer, kidney dysfunction, and hypertension (Satarug *et al.* 2003). These studies suggest that the NOAEL for cadmium may be substantially less than 10 $\mu g \cdot kg^{-1} \cdot day^{-1}$ used to derive the reference dose and that the current reference dose may be too high.

Risk Characterization

Table 1 illustrates that a TDI of 0.2 $\mu g \cdot kg^{-1} \cdot day^{-1}$ is calculated for non-indigenous Canadians who do not consume oysters. This cadmium intake approximates the Agency for Toxic Substances and Disease Registry (ATSDR) chronic oral minimal risk levels (MRL) of 0.2 $\mu g \cdot kg^{-1} \cdot day^{-1}$ (ATSDR 1999) and corresponds with a hazard index (HI) of approximately 0.2, *i.e.*, less than 1.0. Based on a consumption rate of 12 oysters per month and using the USEPA reference dose ($R_fD = 1\ \mu g \cdot kg^{-1} \cdot day^{-1}$), cadmium intake is approximately 0.84 to 1 $\mu g \cdot kg^{-1} \cdot day^{-1}$ for non-smokers and 0.9 to1.06 $\mu g \cdot kg^{-1} \cdot day^{-1}$ for smokers. This cadmium intake is 4- to 5-fold greater than the ATSDR chronic oral minimal risk levels (MRL) and corresponds to hazard indices in oyster consumers of approximately 0.84 to 1 for non-smokers and 0.9 to 1.06 for smokers. This suggests that the current recommended maximum oyster consumption rates are consistent with the FAO/WHO and USEPA limits for acceptable risk, but leave little or no room for error or uncertainty.

A key source of uncertainty in the derivation of recommendations for oyster consumption lies in the selection of the reference dose. For example, Satarug *et al.* 2000 argued that the FAO/WHO reference dose of 1 $\mu g \cdot kg^{-1} \cdot day^{-1}$ is too high to ensure that renal dysfunction does not occur as a result of dietary Cd intake (Satarug *et al.* 2000). If based on recent studies (Satarug *et al.* 2003) the reference

Table 1. Cadmium exposure from all sources ΣCE in $\mu g^{-1}person^{-1}day^{-1}$; the Tolerable Daily Intake TDI in $\mu g{\cdot}kg^{-1}{\cdot}day^{-1}$; the Agency for Toxic Substances and Disease Registry (ATSDR) chronic oral minimal risk levels (MRL) and the calculated Hazard Index (unitless) for a cultured BC oyster consumption of 12 oysters per month using the FAO/WHO reference dose of 1 $\mu g^{-1}.kg^{-1}day^{-1}$ and a suggested lower reference dose corresponding to observed effects concentrations.

	Non-oyster consumers and non-smoker	Oyster consumers and non-smokers	Oyster consumers and smokers
Cadmium Exposure ($\mu g{\cdot}person^{-1}{\cdot}day^{-1}$)	14	59–70	63–74
TDI ($\mu g{\cdot}kg^{-1}{\cdot}day^{-1}$)	0.20	0.84–1	0.9–1.06
MRL ($\mu g{\cdot}kg^{-1}{\cdot}day^{-1}$)	0.20	0.20	0.20
HI for R_fD of 1 $\mu g{\cdot}kg^{-1}{\cdot}day^{-1}$	0.20	0.84–1	0.96–1.06
HI for R_fD of 0.5 $\mu g{\cdot}kg^{-1}{\cdot}day^{-11}$	0.40	1.68–2	1.8–2.12

dose is adjusted to 0.50 μg Cd.$kg^{-1}{\cdot}day^{-1}$, *i.e.*, the cadmium intake rate at which toxicological effects have been observed and hence assuming no adjustment for uncertainty through an uncertainty factor (*i.e.*, UF = 1.0). In Table 1 are shown that the hazard indices for oyster consumers at the maximum recommended oyster consumption rate of 12 oysters per month increase to approximately 1.68 to 2 for non-smokers and 1.8 to 2.12 for smokers, indicating potential for effects.

Another key source of uncertainty is the large variation in cadmium intake and exposure through sources other than consumption of oysters among sub-populations. This variability can cause certain parts of the Canadian populations to be at a considerably higher risk than others at the same rate of oyster consumption. For example, women who are subject to iron, zinc, or calcium deficiencies are subject to higher intestinal absorption rates of cadmium salts and an increased cadmium deposition in the kidney (Ohta and Cherian 1995). Other people in "high-risk groups" are those who have a renal impairment from diabetes (Satarug *et al.* 2000) causing twice the risk of tubular dysfunction in kidney cortex than the normal population (Jarup *et al.* 1998a). Sub-populations at possibly the greatest risk are those who consume caribou and moose organ meats, which contain exceptionally high cadmium concentrations.

Using the lower suggested reference dose of 0.50 $\mu g{\cdot}kg^{-1}{\cdot}day^{-1}$, the hazard index falls below 1.0 if oyster consumption rates are less than 6 oysters per month. To remain below the ATSDR chronic oral minimal risk levels (MRL) of 0.2 $\mu g\ kg^{-1}\ day^{-1}$, the oyster consumption rate needs to be further reduced to 2 to 3 oysters per month.

It may be argued that oysters are only a minor or seasonal component of the diet. However, the New Zealand Total Diet Survey of 2000 (Vannoort *et al.* 2000) concluded that five foods within a "typical" diet contributed 72% of the cadmium intake. These foods are oysters (40%), potatoes (14%), breads (13%), silverbeet

(3%) and carrots (2%). Mean renal cortex cadmium concentrations at age 50 in Canada ranges between 25 and 100 $\mu g \cdot g^{-1}$ wet weight (LeBaron *et al.* 1977) for individuals not exposed to excessive amounts of cadmium. In Europe, current average concentrations of cadmium in the renal cortex in the general population at the age of 40 to 60 years range between 15 and 40 $\mu g \cdot g^{-1}$ (WHO 2000). Considering that the critical level associated with increased risk of bone fracture, cancer, kidney dysfunction, and hypertension is approximately 50 $\mu g \cdot g^{-1}$ wet weight (Satarug *et al.* 2003; Hotz *et al.* 1999), it appears that there is only a small safety margin between cadmium exposure in the normal diet and exposures that could produce deleterious effects.

It is therefore important that human consumption guidelines appropriately and cautiously consider the hazards of cadmium exposure in high risk groups such as smokers, women with low blood iron content, children, individuals with renal impairment, and people habitually eating a diet rich in cadmium, such as farmed oysters or game meats.

CONCLUSION

This study indicates that based on currently available data, Health Canada's recommended BC-cultured oyster consumption rate of 12 oysters per month can be expected to cause a cadmium intake rate of approximately 0.84 to 1 $\mu g \cdot kg^{-1} \cdot day^{-1}$ for non-smokers and 0.9 to 1.06 $\mu g \cdot kg^{-1} \cdot day^{-1}$ for smokers. This cadmium intake rate exceeds the ATSDR chronic oral minimal risk levels (MRL) of 0.2 $\mu g \cdot kg^{-1} \cdot day^{-1}$ (ATSDR 1999) by approximately 4- to 5-fold and reaches the FAO/WHO reference dose of 1 $\mu g \cdot kg^{-1} \cdot day^{-1}$ for cadmium consumption for Canadians. This suggests that while the current recommended maximum oyster consumption rates is consistent with the FAO/WHO and USEPA limits for acceptable risk, it leaves little or no room for error or uncertainty.

This study notes recent studies indicating toxicological effects of cadmium at exposure levels of 0.43 to 0.71 $\mu g \cdot kg^{-1} \cdot day^{-1}$. This indicates that the current FAO/WHO reference dose may be too high. If the reference dose is lowered, the BC-cultured oyster consumption rate should be lowered substantially.

There are several sub-populations that are at higher risks of cadmium toxicity than the general population. These subpopulations include women with low iron store, people with renal impairment, smokers, children and indigenous people who smoke and consume internal organs of games and wildlife other than shellfish. Lower cultured oyster consumption rates should be recommended for people in these high-risk groups. It is possible that the high-risk groups comprise a substantial portion of the population. Indigenous Canadians are amongst the highest risk sub-populations due to the reliance on country foods, such as organ meats, moose, caribou, and whitefish. The potential health effects in this sub-population are beyond the scope of this study but merit additional attention.

Several international bodies such as the European Union (EU), United Nations Food and Agriculture Organization/World Health Organization (FAO/WHO), Codex Alimentarius Commission (CODEX) and Australia New Zealand Food Authority (ANZAF) are considering lowering the limit of 1 $\mu g \cdot g^{-1}$ (Kruzynski 2002). Canada should consider stipulating its own acceptable limit to 1 $\mu g \cdot g^{-1}$ and attempt to further

investigate the cause of oyster cadmium contamination in farmed BC oysters and implement corresponding management strategies to reduce cadmium concentrations considering that cultured oysters appear to contain higher Cd concentrations than wild oysters from nearby sites (Kruzynski 2000).

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