Investigation of Elevated Blood Arsenic Blackville New Brunswick December 2008 to February 2009

TRIP REPORT

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Executive Summary

In the fall of 2008 federal Field Epidemiologists were asked to assist in an investigation after four individuals with elevated blood arsenic were discovered in Blackville, New Brunswick (NB). The investigation consisted of four components: hazard assessment, case finding, exposure assessment and environmental investigation.

Medical reviews revealed that none of the initial persons under investigation met the case definitions for probable or confirmed cases. A thorough exposure history of these four persons did not reveal any dietary, household, occupational or recreational/hobby exposures associated with toxic arsenic exposure.

None of the 65 community members whose laboratory tests were reviewed met the case definition for arsenic toxicity. All persons submitting urine specimens had inorganic arsenic levels within normal limits.

All arsenic well water samples taken in Blackville during the investigation were below the Guideline for Canadian Drinking Water Quality (0.01 mg/L). No environmental or industrial sources of arsenic were identified within the village of Blackville and the area geology is not associated with arsenic-containing rocks.

With the possible exception of the index individual whose diagnostic investigation remains in progress, no evidence of arsenic toxicity was found among any community members who underwent testing and whose results were reviewed by the investigative team. The investigative team concluded that arsenic does not pose a threat to this community.

Introduction

In early September 2008, a family physician alerted the regional Medical Officer of Health (MOH) Region 7 and the Royal Canadian Mounted Police (RCMP) in New Brunswick to the possibility of arsenic toxicity. Three related adults had elevated levels of total arsenic in their blood; one had symptoms compatible with arsenic toxicity. On October 17, 2008 this physician requested assistance from public health to identify the arsenic source and provide toxicology advice to area physicians. Public health distributed an arsenic information package to local physicians in mid-November to increase diagnostic suspicion and encourage testing of symptomatic patients. A fourth asymptomatic adult with elevated blood arsenic subsequently came to light, reported by another physician. These four persons under investigation lived in three adjacent houses; interviews by a Public Health Inspector did not identify a source and well water results were all negative for arsenic. Community concern led to the issue being raised by the local Member of the Legislative Assembly, and in response on November 26, 2008 the NB Minister of Health offered free well water testing for arsenic to Blackville residents living in the neighborhood of the three adjacent homes.

The village of Blackville is located on the Miramichi River and has population of 931 (NB Dept of Finance 2006). The land along the Miramichi River (including the village of Blackville) is mostly forested (NB Department of Environment a). There are many private woodlots with the remainder of the land managed by the NB Department of Natural Resources, primarily to support the pulp and paper industry via timber leases to forestry companies. There is very little crop farming (potatoes, turnips, oats, wheat); berry cultivation and dairy farming are also practiced.

The Health Protection Branch, New Brunswick Department of Health requested Field Epidemiologist assistance from the Public Health Agency of Canada (PHAC), to identify the source of the arsenic and suggest appropriate risk reduction strategies. These objectives would be fulfilled in collaboration with clinicians, local and provincial public health and environmental departments, and Health Canada's Healthy Environments and Consumer Safety Branch (HECSB).

Background

Arsenic is a naturally occurring element found in many geological formations worldwide, particularly those that contain copper, lead, cobalt and gold (ATSDR 2007). On a global scale, most exposure to naturally occurring inorganic arsenic is through drinking contaminated well water (e.g., in parts of Bangladesh, Taiwan, and South America; ATSDR 2007, Chiu et al. 2004, Ferreccio et al. 2000, Mead 2005). However, in Canada, drinking water is a relatively rare inorganic arsenic source, restricted to areas of geological or human contamination (Health Canada 2006). For most of the general Canadian population, food is the most important source of inorganic arsenic (ATSDR 2007, Equilibrium Environmental Inc. 2008).

Anthropogenic sources of inorganic arsenic include mining, smelters, commercial production of the wood preservative copper chromated arsenate (CCA), and manufacturing some metal alloys (e.g., lead-acid batteries, semiconductors and light-emitting diodes). Historically, inorganic arsenic was used in pesticides for agriculture (cotton, orchards, and potatoes) and food storage (ATSDR 2007).

Inorganic arsenic present in the soil from mining, industry or historical application as pesticides may pose a danger through direct ingestion (particularly for young children; ATSDR 2007; Health Canada 2006) or ingestion of food crops (ATSDR 2007; Kapaj et al. 2006; Mead 2005). Chronic exposure through air and/or soil contaminated from nearby sources of industrial arsenic releases may also result in toxicity. Some medicines and natural supplements may also contain inorganic arsenic (ATSDR 2007; Amster 2007). Inhalation of inorganic arsenic during occupational exposures at ore smelters and burning or sawing CCA-treated wood may result in acute or chronic toxicity (ATSDR 2007). Direct absorption through the skin is unlikely, since arsenic is not readily absorbed through this route (ATSDR 2007).

Seafood and other foods may contain high levels of trimethyl organic arsenic (food arsenic, e.g., arsenobetaine and arsenocholine), which is considered to be non-toxic to humans, unlike inorganic arsenic and its two organic metabolites (monomethyl arsenic, MMA and dimethyl arsenic, DMA ATSDR 2007) (Appendix A). Other organic arsenic compounds are used as anti-microbials and growth promoters in animal feeds (e.g., roxarsone, arsinilic acid; Lasky et al. 2004).

Acute ingestion of inorganic arsenic produces irritation of the stomach and intestines causing nausea, profuse watery or bloody diarrhea and vomiting. Patients may have low blood pressure, high heart rate and a drop in blood cell count. Severe poisoning either by ingestion or inhalation can lead to delirium and death.

Effects of chronic exposure can include: hyperpigmentation and keratosis, various cancers of the skin, internal organs and lungs, altered kidney and liver function, cardiovascular disease, neuropathy, and altered cognitive function (Appendix B).

Arsenic toxicity is rare in Canada largely due to regulation of its use in situations where exposure could occur. For example, the federal government recently released the Guideline for Canadian Drinking Water Quality which includes limits for arsenic (Health Canada 2006). Under the Canadian Environmental Protection Act, risk management measures focusing on base metals smelters, steel manufacturing facilities, electric power generation facilities, and wood preservation facilities have determined release reduction targets for metals including arsenic. The Metal Mining Liquid Effluent Regulations under the federal Fisheries Act have also been promulgated to restrict releases of arsenic and other metals in mine effluents. Inorganic arsenic is no longer used as a pesticide on agricultural crops and changes to smelting techniques since the 1980s have reduced arsenic emissions from smelters (ATSDR 2007). In 2002 Canadian wood manufacturers agreed to voluntarily phase out CCA in residential uses such as decking and playgrounds (Health Canada 2003).

In addition to the Guideline for Canadian Drinking Water Quality, Health Canada and Environment Canada have set federal guidelines for arsenic in soil and air. Canadian jurisdictions can use these guidelines when establishing provincial requirements. The New Brunswick Department of Health has adopted the Health Canada guideline for arsenic in drinking water (0.01 mg/L), and uses the soil guideline from the Canadian Council of Ministers of the Environment (12 ppm) when assessing risk for residential, park, agricultural, commercial and industrial lands. New Brunswick refers to the Ontario Ministry of Environment standard for ambient air (24 hour average 25 ug/m3).

Occupational standards require frequent testing of workers who may be exposed to inorganic arsenic and mitigation if exposure is above accepted levels. Many biomonitoring tests are available for arsenic (e.g., blood, urine, hair, nails) but they must be interpreted carefully. The laboratory usually sets "positive" and "negative" values for total arsenic in blood, based not on toxicity but rather to indicate that further testing for inorganic arsenic fraction in urine is required; elevated blood levels may be a frequent occurrence in many people, particularly if they have recently consumed certain foods. For example, consumption of seafood within 2 to 3 days of urinary tests for arsenic can elevate total arsenic in blood and urine several fold (ATSDR 2007). Even laboratory values for inorganic arsenic do not clearly distinguish toxic and non-toxic levels, since there is considerable variability in arsenic metabolism and subsequent symptoms (Lindberg et al 2007; Vahter 2000). Therefore, once exposure to a potentially toxic form of arsenic has been established for a given patient, the confirmation of illness attributable to arsenic requires assessment by a physician experienced in the diagnosis of arsenic toxicity.

Confirmed inorganic arsenic toxicity may be treated with chelation. Chelating agents are charged molecules that bind to metals, causing them to be removed from stable body stores such as bones and be excreted in the urine. Restricting the patient's inorganic arsenic exposure stops the immediate danger of further intoxication and chelation therapy can remove some arsenic from the body, but some symptoms may not be reversible (Hall 2002; Mukherjee et al. 2003).

Methods

This investigation consisted of four components: hazard assessment, case finding, exposure assessment and environmental investigation. The investigative team developed an algorithm to guide the investigation based on a literature review (Appendix C).

Hazard assessment

The investigative team reviewed the literature to assess adverse health effects associated with arsenic exposure. This included characterization of the agent, acute and chronic health effects, vulnerable populations, doseresponse and biomonitoring. We also summarized the areas of uncertainty and limitations of the data.

Case finding

Case finding in this investigation consisted of developing case definitions based on a literature review, validating the four initial persons under investigation, and active surveillance for cases in the community.

Case definitions

The investigation team developed the following case definitions: cases are individuals of any age residing or working in Blackville since January 1, 2006 with the following characteristics:

Persons under investigation: blood, spot urine or 24-hour urine total arsenic above the normal range¹

Suspect: inorganic arsenic in 24-hour urine above 25 umol/mol Cr²

Probable: inorganic arsenic in 24-hour urine above 25 umol/mol Cr AND symptoms compatible with arsenic toxicity (see Appendix B)

Confirmed: inorganic arsenic in 24-hour urine above 25 umol/mol Cr AND symptoms compatible with arsenic toxicity (see Appendix B) AND diagnosis of arsenic toxicity by a physician specializing in heavy metal toxicities

Case validation

The four initial persons under investigation were discovered by their family physicians and an alternative health practitioner. The latter diagnosed the symptomatic index patient using a provocation test, where urine is tested for heavy metals after administration of a chelating agent and analyzed in an American laboratory. Two other family members were tested and had elevated total blood arsenic noted by their family doctors in August 2008 and November 2008 respectively. The fourth individual approached their family doctor for testing after learning about the others, and had elevated total blood arsenic noted in November 2008.

Case validation, conducted between December 7 and 11, 2008 after obtaining informed consent from the four persons under investigation, included medical history interviews, medical chart review, interviews with local physicians and an alternative health practitioner, and review of biomonitoring results.

The investigative team developed a medical history questionnaire (Appendix D), and administered it in face-to-face interviews conducted by the Field Epidemiologists with the four individuals in December 2008. Although there are no definitive risk factors for arsenic toxicity defined in the literature, we paid particular attention to risk factors currently under investigation because they may modify arsenic metabolism: male sex, smoking and alcohol consumption, micronutrient and macronutrient deficiencies (e.g., vitamin B12, iron, zinc, niacin, protein; Hsueh et al. 2003; Lindberg et al. 2007; Steinmaus et al. 2005; Appendix E).

We reviewed medical records and biomonitoring conducted by both family physicians and alternative health practitioner and interviewed these clinicians. We also requested a review of the medical history of the index individual by Dr. Gideon Koren, Director of Motherisk Programs, Clinical Pharmacology and Toxicology and Professor of Pediatrics, University of Toronto.

Expert advice was solicited from the Hospitals in Common Laboratory, London, Ontario regarding the most appropriate test to determine arsenic exposure in non-occupational populations, particularly those undergoing chelation therapy. Since no population norms exist for arsenic biomonitoring under chelation conditions, the investigative team developed a testing protocol to eliminate the effects of chelation and the major source of food arsenic. Patients stopped chelation after January 7, 2009 and ceased all fish/seafood consumption. A telephone call one week prior to testing reminded them of their upcoming test and highlighted the importance

Laboratory testing was conducted by the Hospitals in Common Heavy Metals Laboratory in London, Ontario using inductively coupled plasma mass spectrometry (ICP-MS). For total arsenic, a value above the normal range does not necessarily indicate toxicity, but rather is a low cut-off at which speciated testing of the urine should be done to establish the level of inorganic arsenic.

of abstinence from fish/seafood. Twenty-four hour urine and blood samples were collected for testing of total and inorganic arsenic between January 21 and February 11, 2009.

Active case finding

Community case finding began in mid-November 2008 with a letter from the MOH Region 7, to area physicians to alert them of the possibility of arsenic toxicity and encourage testing of symptomatic patients. This approach was refined with a second letter on December 8, 2008 (Appendix F) to inform physicians of the optimal specimen collection for patients with symptoms compatible with arsenic toxicity (i.e., a spot first morning urine sample after a one week seafood abstinence, with the inorganic fraction measured if the total arsenic result was above 25 nmol/L).

The investigative team requested that similar testing be done for any residents found to have high levels of arsenic in their well water, particularly those living in close proximity to the four initial persons under investigation. Children of these four persons, even those who did not live in Blackville, were asked about symptoms and spot first morning urine tests were requested.

Both symptomatic and asymptomatic Blackville residents sought arsenic testing from their family physicians.

Retrospective case finding was also conducted to look for unexplained deaths and/or increases in deaths/ hospitalizations due to conditions associated with arsenic toxicity in Blackville residents using existing data sources. Data was obtained from NB Vital Statistics regarding the number of deaths in Blackville residents in 2002-2006 from the following causes using ICD-10 codes: squamous cell cancer, Bowen's disease, hepatocellular cancer, renal cell cancer, lung cancer, myelogenous leukemia, Hodgkin's disease. Anecdotal reports of suspicious deaths were also followed up.

In addition, the investigative team reviewed the NB Hospital Finance and Utilization Database for hospital admissions of Blackville residents in 2002-2006 for the following causes: lung cancer, kidney cancer, non-melanoma skin cancer, bladder cancer, secondary liver cancer, myeloid leukemia, Bowen's disease, Hodgkin's disease, polyneuropathy, dermatitis due to other causes, toxic effects of metals, toxic effects of arsenic, poisoning due to pesticides. ICD-9 codes were used from 2002-2003 and ICD-10 codes were used from 2004-2006.

Exposure assessment

Investigating sources of arsenic exposure for the initial persons under investigation
Results of medical chart reviews and interviews were examined to construct a timeline of symptoms to determine possible exposure period(s).

A hypothesis-generating exposure assessment questionnaire (Appendix G) was developed based on an existing NB arsenic survey tool and a literature search of natural and anthropogenic arsenic sources. The questionnaire included a detailed occupational history, travel and leisure activities, food history and home environment and was administered to the four individuals via face to face interviews with the Field Epidemiologists between December 7 and 11, 2008.

All historical residential well water results for arsenic were reviewed for the three adjacent houses.

On the recommendation of a contracted occupational hygienist who did an initial assessment of one of the three houses in October 2008, a private company Research and Productivity Council (PRC) performed a trace metals environmental assessment of this house in November 2008. Although public health was not involved in the decision to hire these professionals, the investigation team obtained consent to review the findings and RPC was contacted to establish testing criteria and methodology. A walk through environmental scan of this house was conducted on December 12, 2008 by the Field Epidemiologists.

A list of personal and household hygiene products used by all four people was compiled and forwarded to HECSB regarding any consumer complaints and/or product testing results for arsenic.

Based on common exposure information obtained through the exposure assessment questionnaire, the investigative team requested that the Canadian Food Inspection Agency (CFIA) test selected food items from

Restaurant A for arsenic at the CFIA laboratory in Halifax, Nova Scotia. On January 6, 2009 a NB Public Health Inspector and a CFIA inspector collected samples of the food items used to make fish and chips: frozen haddock loins (commercially distributed Highliner brand), cooked haddock coated with homemade batter; and the cooking oil. The frozen fish sample tested was a composite sample of five individual loins.

Investigating sources of arsenic exposure in the community

Discussions were held with key Blackville residents (e.g., mayor, town councilors, and community elders) regarding the current and historical use of arsenic in the area, particularly the historical land use around the three adjacent houses.

A historical review was conducted of the industries in Blackville and Miramichi River watershed, focusing particularly on mining, smelting and lumber mills. Information was obtained on historical use of wood preservatives/chemicals used for wood treatment in local sawmills, particularly the possible use of arsenic at the mill in neighboring Doaktown.

Google Earth was used to look for undeclared industrial and mining sources in the watershed area.

The village of Blackville was mapped to identify the locations of the three houses, vulnerable populations and potential current and historical sources of exposure for the community.

Environmental investigation

Water

On November 26, 2008 in response to community concerns, the NB Health Minister offered free inorganic arsenic well water testing to homes surrounding the index houses. The results of these tests were reviewed and the location of all Blackville wells tested for arsenic was mapped.

Since 1999 it has been mandatory in NB to test all new wells for inorganic arsenic. The Blackville schools and medical centre are also tested annually. These historical well water results were reviewed by the investigative team. Inquiries were also made to the NB Department of the Environment to obtain historical ground water data for arsenic in the Blackville area prior to the public release of the NB Ground Water Atlas.

Fish

The investigation team liaised with the NB Department of Natural Resources to obtain a list of edible fish species in Miramichi River and historical data from fish testing in the Miramichi watershed was collated. The team consulted CFIA and the NB Farming Salmon Association regarding routine testing of the salmon research station and hatchery in Miramichi. The Department of Fisheries and Oceans, NB Department of Natural Resources, and Miramichi Salmon Association were asked to provide data on the testing of freshwater fish in the Miramichi watershed. We also reviewed reports from the Miramichi River Environment Committee (MREAC) for arsenic testing results of fish (Michael and Chadwick, MREAC 2007).

Soil

The investigation team contacted officials at Miramichi Regional Hospital (operator of Blackville Medical Clinic) for any soil test results prior to the construction of the clinic. Inquiries were made to the NB Department of Environment regarding a sand pile and possible runoff from heavy equipment stored on a nearby property.

The NB Department of Natural Resources was contacted regarding till and soil geochemistry for the Blackville area and bedrock maps were reviewed.

We liaised with the NB Department of Natural Resources and the NB Department of the Environment to obtain results of sediment testing for arsenic in the Miramichi watershed. MREAC reports were reviewed for arsenic testing results of sediment in the Miramichi River (Michael and Chadwick, MREAC 2007).

Data analysis

Questionnaire and chart review data collected during the investigation are filed in a secure location. The questionnaire data was summarized manually and these findings entered into Microsoft Office Excel 2003 spreadsheets. Timing of biomonitoring and chelation therapy was compared using Microsoft Excel 2003 spreadsheets and graphing functions. Community laboratory results were stripped of identifiers and entered into a Microsoft Office Excel 2003 spreadsheet and analyzed using Excel. Maps were constructed using Microsoft Office PowerPoint 2003 and Microsoft Office Paint 2003.

Results

Although most environmental investigations validate the index case(s)' diagnosis before proceeding with risk assessment (hazard characterization, exposure investigation, environmental investigation), the investigation team decided that the potential severity of the problem and the level of community concern warranted conducting case validation and risk assessment concurrently.

Hazard characterization

Although arsenic is widely known as a poison, not all forms of arsenic are harmful. Inorganic arsenic and its two organic metabolites (MMA, DMA)³ are all considered toxic to human tissues (ATSDR 2007). Appendix H shows the metabolic pathway of inorganic arsenic.

In order to identify cases of arsenic toxicity, it was important for the investigative team to establish the appropriate interpretation of biomarkers. Table 1 shows that total arsenic measured in both blood and urine includes both the inorganic and organic arsenic species. However, only urinary arsenic can be speciated into the organic and inorganic fractions. Therefore the definitive test for the assessment of exposure to inorganic arsenic is 24 hour urine collection. If total blood arsenic or first morning spot urine is elevated, then the individual should abstain from seafood consumption for 2-3 days and subsequently collect 24 hour urine for speciation to distinguish between elevations of the inorganic or organic fraction (Hughes 2006).

Table 1. Species of Arsenic Included in Results for Specimens Tested at Hospitals-in-Common Heavy
Metals Laboratory, London ON

Specimen	Inorganic Arsenic	Methylated Arsenates	Food Arsenics
Blood – total arsenic	х	x	х
Urine – total arsenic	х	х	Х
Urine – inorganic arsenic	х	х	-
X Included in this arsenic fraction - Not included in this arsenic fraction			

Case finding

Case validation

Epi-links were quickly established among the four initial persons under investigation. All had elevated total blood arsenic levels prior to December 2008, but of those who applied the definitive test (24-hour urine collection for speciated arsenic after abstaining from fish/seafood), none had elevated levels of inorganic arsenic.

The medical chart review of the individuals treated with chelation revealed consistently low levels of inorganic arsenic every time they were tested. Interviews with the family physicians and the alternative practitioner, review

³ MMA and DMA are methyl arsenates. Since they consist of arsenic combined with hydrogen and carbon, they are 'organic' species. However, this subtlety is often simplified in the literature, so that MMA and DMA are under the umbrella term 'inorganic'. In biomonitoring, MMA and DMA are usually included in the inorganic fraction whereas arsenocholine and arsenobetaine are in the organic fraction.

of the medical history of the index individual by a physician specializing in heavy metal toxicity, and personal interviews revealed that none of the persons under investigation met the case definitions for probable or confirmed cases.

Active case finding

All 37 well water results for neighboring residents revealed low or non-detectable levels of arsenic, therefore follow up urine sampling was not required. Two adult children of the original family cluster lived in a different NB region; they reported no symptoms and their urine total arsenic was within normal limits.

As a result of the MOH's letters to family physicians, at least one of the community members tested was symptomatic; the inorganic result was low and the patient was diagnosed with another medical condition.

Community concern prompted many asymptomatic persons to seek testing by their family physicians. As of February 12, 2009, public health received laboratory results for 65 Blackville residents (excluding the 4 initial persons under investigation) for specimens collected between November 25, 2008 and February 2, 2009. Females (60%) outnumbered males (40%); however the average age for males was slightly higher (40.6 years) than for females (37.6 years). The age range for all sexes was 2 to 78 years of age, with 10 (15.4 %) being children aged 10 years and younger.

Not all persons received definitive testing for inorganic arsenic toxicity. 42% had urine tests; 57 (88%) of individuals had blood tests, 6 (9%) had hair samples taken and 2 (3%) had nail samples (Appendix I).

Of the 27 persons (42%) who submitted 24 hour or spot urine tests, total arsenic results ranged from 3.4 to 911.4 umol/mol and 9 (35%) had elevated levels. However, all 27 individuals had inorganic arsenic levels within normal limits (less than 25 umol/mo Cr; 5/27 did not have urine speciated for inorganic arsenic as total urine arsenic was within normal limits). Of the 57 individuals with blood results, the total blood arsenic levels ranged from 1.3 to 395.20 nmol/L and 53% (30/57) had total arsenic blood levels greater than the cutoff value of 21.4 nmol/L set by the laboratory. Of the 30 with elevated total blood levels, 11(36.6%) had urine speciated for inorganic arsenic: all were within normal range. Arsenic levels of the six hair samples ranged from 0.1 to 0.7 which are below the reference cutoff value of 2.0 nmol/gm. Both nail samples were an order of magnitude below the reference cutoff value of 6.68 nmol/gm. None of the 10 children aged 10 years and younger had arsenic levels (blood, urine or hair) above normal limits.

Examination of NB Vital Statistics data for deaths possibly due to remote arsenic exposure revealed the number of lung cancer deaths among Blackville area women between 2002 and 2006 was higher than would be expected based on the provincial average (Appendix J). An anecdotal report of a suspicious death was reported and investigated: some community members were concerned that a neighbor of one of the persons under investigation had died suddenly in the summer of 2008 from arsenic toxicity. The individual's family physician stated that this death was attributable to a pre-existing medical condition, unrelated to arsenic toxicity.

A review of hospital admissions for Blackville residents in 2002-2006 for a select number of ICD-9 codes associated with possible chronic arsenic exposure, revealed 1,814 admissions, none suggestive of arsenic intoxication.

In summary, the case finding done in the community discovered 33 persons with elevated total blood or urine arsenic levels, but of those who applied the definitive test (24-hour urine collection for speciated arsenic), none had elevated levels of inorganic arsenic.

Exposure assessment

Investigating sources of arsenic exposure for the initial persons under investigation

No occupational exposures to inorganic arsenic were discovered, with the possible exception of volunteer firefighting which may have led to inadvertent exposure to fumes from products containing arsenic. However, symptom onset from the time of this exposure was unduly prolonged. No exposures to inorganic arsenic through travel, leisure activities, food history, or home environment including personal and household products were discovered for the four individuals.

Recent and historical testing of 33 well water samples of the three households were all below detectable levels for arsenic. Review of the contractor's air, water, household items and structural sampling in 2008 did not reveal any sources of elevated arsenic in the home.

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All four individuals ate fish and chips from Restaurant A. Testing by CFIA found the following arsenic concentrations: frozen haddock 30 parts per million (ppm), cooked battered fish 17 ppm and cooking oil 0.018 ppm. Calculations were made to determine if these levels posed a possible health risk. Assuming two to ten percent of total fish arsenic is inorganic and an average daily fish consumption of 40 grams/day (Health Canada 2007) a 70 kg person eating haddock with 30 ppm total arsenic would receive a dose of 0.34 to 1.71 ug/kg per bw/day of inorganic arsenic, which is less than the provisional tolerable daily intake limits (PTDI) of 2.14 ug/kg bw/day set by the World Health Organization (Health Canada 2009).

Investigating sources of arsenic exposure in the community

Exploring the historical land use in Blackville area revealed that the current council building was once a general store with grain storage where the current Blackville Medical Clinic is located. Anecdotal stories describe frequent use of rat poison (likely containing arsenic). The area in front of the Medical Clinic is a paved parking area.

There were two former dump sites within the village of Blackville (Appendix K). The large municipal dump site operated between 1966 and 1971. In August 2002 the NB Department of Environment contracted Gemtec Ltd. to make an environmental study of the closed site. The study concluded that the former dump site had a low potential for affecting the environment. All soil samples were below the limit of quantification (LOQ) for arsenic, the upstream brooks had arsenic levels below 1.0 ug/L and surface water had an arsenic level of 1.6 ug/L which were below the Guideline for Canadian Drinking Water Quality. The second smaller site was not an official dump site.

Blackville hosted two lumber mills in the past: one which operated at the site of the current playground and another larger mill (UPM) which closed in the spring of 2008. Both mills used chemical solutions to debark logs which was said to have been dumped out on the ground. Arsenite has been used as a debarking agent in forestry in the past but the current mill owners and the Department of the Environment have no knowledge of arsenic being used to treat wood in Blackville. The mayor stated that a Borox solution (containing sodium and borate, not arsenic) was used at both mills.

The town of Miramichi has had several lumber and pulp and paper mills since the late nineteenth century. The Weyerhauser board mill closed early in 2007 and the last operating mill (UPM) closed in December 2007. The UPM mill had a hot pond where chemicals were used to debark logs but the chemicals' identity is unknown. Doaktown is upriver from Blackville and also has a long history of lumber mills, including a currently functioning saw mill which likely had a tank for debarking logs.

A mine had been located at the headwaters of the Tomogonops and Little Rivers, 60 km northwest of Miramichi (1956-1999). No smelter was included in the facility but it was a large productive underground mining and milling operation of copper, lead and zinc. There were occasional breaches of the holding tanks resulting in fish kills in the river in 1960 and 1991. The Tomogonops River empties into the Miramichi River downstream of Blackville. The area around this former mine is forested with few residential properties; there are no records of wells tested for inorganic arsenic in the area.

Aerial spraying for spruce bud worm occurred in NB around 15 years ago using two non-arsenic containing pesticides: Fenitronthion (an organophosphorus insecticide) and Bacillus thuringiensis (a biological insecticide). Ground/aerial herbicides used in forest plantations are based on glyphosates, not arsenic.

Google Earth had insufficient resolution to detect undeclared industrial and mining sources in the Miramichi watershed area.

Environmental investigation

Water

Between November 25 and December 3, 2008, 37 Blackville homeowners had their wells tested and all arsenic results came back below detectable limits (Appendix L).

A review of 30 historical water testing data for arsenic in the Blackville area including the Medical Clinic and the school revealed that all were below the Guideline for Canadian Drinking Water Quality for arsenic and the majority (94%) was below detectable limits.

The NB Groundwater Chemistry Atlas (Department of Environment (b)) contains arsenic levels for all wells tested between 1994-2007. In the Blackville area there is one well northwest of the community which had a result of 0.0127 mg/L which exceeds the Guideline for Canadian Drinking Water Quality of 0.01 mg/L (Appendix M)

Fish

NB Department of Natural Resources listed the following edible fish species found in the Miramichi River: striped bass, shad, gaspereax, rainbow smelt, Atlantic salmon, trout, eels, and suckers. Department of Fisheries and Oceans, NB Department of Natural Resources, and the Miramichi Salmon Association concurred that arsenic testing of freshwater fish in the Miramichi watershed has not been done. Similarly, there has not been any testing of wild Atlantic salmon in the Miramichi or elsewhere on the East Coast, including the Miramichi mill effluent monitoring as salmon are migratory and are transient in the river. CFIA does not conduct heavy metal testing on Atlantic salmon as there is no commercial fishery or processing.

Both CFIA and the NB Farming Salmon Association stated that fish from the research station and salmon hatchery in Miramichi were routinely tested for heavy metals including arsenic and the results are acceptable.

Soil

The operator did not have any record of soil testing prior to the Medical Clinic's construction.

Community members had raised concerns concerning an industrial property with a pile of sand/gravel used for road maintenance and storage for trucks and machinery. The Department of the Environment stated they have not received any complaints regarding the property and do not consider the heavy equipment or property use to be an environmental issue.

The underlying geology of the Blackville Village area is mainly Late Carboniferous (Minor Triassic to Cretaceous) which is comprised of terrestrial sedimentary rocks. (Department of Natural Resources) (Appendix N). Naturally occurring arsenic is not associated with this type of bedrock.

A review of reports provided by the MREAC did not provide any evidence that water and/or sediment in the Miramichi river waterway were tested for arsenic. Sediments have been tested for other heavy metals but not arsenic.

Discussion

This epi-linked cluster of four adults with elevated total blood arsenic prompted an investigation by the local public health authority with consultation provided by provincial and federal authorities. The investigative team focused on verifying cases and assessing population risks through active case finding, exposure investigation, and environmental investigation. None of the Blackville community members tested met the case definition for arsenic toxicity.

Non-occupational arsenic toxicity is not a common problem encountered in clinical practice. Physicians could benefit from access to a specialist for interpretation of the myriad laboratory tests for arsenic. In other advanced diagnostic tests, like CT scans, results are conveyed to the ordering physician as a report containing the radiologist's interpretation and often recommendations for further follow up (e.g., repeat scan in 6 weeks for comparison).

The results of this investigation demonstrate why many environmental investigations validate the diagnosis prior to embarking on the four components of risk assessment. In this investigation, a more discriminatory test to distinguish between organic and inorganic arsenic was needed to determine potential toxicity. Once the investigative team could convey to community physicians the optimal approach for arsenic toxicity testing, all persons under investigation were discovered to have low levels of inorganic arsenic. Case definitions are designed to cast the net wide to bring in persons under investigation and subsequently refine the search with more specific criteria. For Blackville residents submitting urine samples, including the initial four persons under investigation, all inorganic arsenic levels were well below both the normal levels used by the laboratory and the cutoffs for action used in occupational exposures (biological exposure index (BEI) for inorganic arsenic 52.9 umol/mol Cr; ACGIH 2001).

Long-term exposure to arsenic is a significant global public health problem (Mandal 2005), and affects several Canadian communities (Health Canada 2006). However, the majority of people with elevated total arsenic levels are not exposed to toxic levels of arsenic; but rather have ingested non-toxic dietary arsenic (ATSDR 2007). Arsenic levels in blood and urine of most Blackville residents tested were at or below levels found in other non-exposed community samples (Appendix O). Blackville residents with total blood or urine arsenic levels higher than other non-exposed population groups had inorganic urine levels within normal limits.

Retrospective community case finding revealed no likely cases of hospitalizations or deaths due to arsenic toxicity in the past 6 years. Due to the small numbers involved the finding of increased lung cancers among Blackville women should be treated with caution. Lung cancer rates for persons living in the entire region of Health Region 7 (includes Blackville) are among the highest in the province; indicating that there is a regional rather than local effect (Appendix P). Examining regional differences in the prevalence of the most common risk factor for lung cancer (i.e., smoking) was beyond the scope of this investigation.

A thorough exposure history for each of the four original persons under investigation did not reveal any dietary, household, occupational or recreational/hobby exposures associated with toxic arsenic exposure. The list of household products was reviewed by HECSB, Health Canada and no products with potentially elevated arsenic were identified. Similarly the fish from a local restaurant did not pose a concern for human health at the levels that we observed.

Chronic arsenic toxicity is rare outside of regions with ground water contaminated with naturally occurring arsenic. In such regions the drinking water is a clear source of exposure (above 100 ug/L inorganic arsenic) and affected individuals usually present with pathognomonic lesions such as skin hyperkeratinization as well as arsenic-associated cancers (Mazumder et al. 2003; Mead 2005). In Blackville, 75 well water samples were taken within the past 10 years in 68 locations and 33 samples were taken from three houses where the initial persons under investigation lived. All of these samples were below the Guideline for Canadian Drinking Water Quality (0.01 mg/L) and the majority were below the limit of detection (<1ug/L). The sole result to exceed the Canadian arsenic guideline on the groundwater chemistry map is located outside the village limits.

In this investigation, there were a number of factors that contributed to community concern. Risk communication theory predicts that in situations of fear, uncertainty, complex scientific results and the perception of delay by public officials lead to community "outrage" (Covello et al. 2001). Within a week of the arrival of the Field Epidemiologists, the MOH could convey to area physicians the appropriate testing protocol. The delay in processing specimens for several weeks due to laboratory technical difficulties led to allegations of a cover up. Although clinical issues are usually the remit of the Regional Health Authority, public health worked with local, regional and provincial political and health leaders to address these concerns. This event highlighted the importance of not only a thorough scientific investigation, but also timely reporting and interpretation of results and explanations of delays.

Limitations

The main limitations of this investigation are: diagnostic uncertainty, the lack of definitive diagnostic criteria for chronic arsenic toxicity, paucity of data related to dietary exposure to arsenic in Canada and the lack of environmental surveillance and public health mandate.

We could not definitively rule out arsenic toxicity in the differential diagnosis for the index person under investigation. Neuropathy associated with arsenic toxicity can be permanent, even if the exposure is removed (Hall 2002; Mukherjee et al. 2003). Therefore a previous exposure to arsenic-containing smoke during firefighting

activities (e.g., CCA-treated lumber, stored pesticides in burning barns/garages or warehouse fires) could have resulted in residual symptoms with the normal inorganic arsenic levels currently observed. However, in cases of arsenic neuropathy reported in the literature the latency is two hours to two years (Mukherjee et al. 2003), which did not fit the interval between potential exposure and symptom onset observed.

If all initial persons under investigation had been exposed to low levels of inorganic arsenic in the past but only one had developed symptoms, then this individual may have had a genetic polymorphism in arsenic metabolism that caused build up of toxic metabolites. There is considerable heterogeneity in the metabolism of inorganic arsenic in the population (Steinmaus et al. 2005). Known genetic polymorphisms that increase susceptibility to arsenic toxicity include anomalies in the methylenetetrahydrofolate reductase (MTHFR) pathways and those which cause increased metabolism to MMA compared with DMA (ATSDR 2007; Brouwer et al. 1992; Steinmaus et al. 2004). If this hypothesis is correct, a metabolic anomaly in one individual would not pose a public health risk to the community.

The "normal" range of total blood arsenic varies between laboratories. The Hospitals in Common Heavy Metals Laboratory which performed the analyses for this investigation uses a narrower (more conservative) normal range than the Direction toxicologie humaine et Direction risques biologiques, environnementaux et occupationnels of the Institut National de santé publique du Québec. Nor is there a widely accepted cut off for inorganic arsenic testing. Among occupationally exposed workers, the biological exposure index (BEI) has been set by the American Conference of Industrial Hygienists at 35 ug/g creatinine (53 umol/mol Cr; ACGIH 2001). This is meant to be an action level for a population of healthy workers. Another commonly used laboratory normal is <25 umol/mol which is used to identify workers who may have been exposed above acceptable levels. Given the variation among individual susceptibility, neither the BEI nor the lower cut off is designed to delineate a 'toxic' or hazardous level of exposure from one that is not hazardous. The diagnostic uncertainty is reflected in our case definitions which include not only symptoms and laboratory findings but also assessment by a physician specializing in heavy metal toxicity.

The wide range in total blood arsenic levels found for community members is most likely due to dietary variations. Although it was recommended that persons be tested after abstaining from seafood for 7 days it is not known how many complied. Although the initial persons under investigation denied eating seafood, the dietary history revealed that all four consumed different types of fish (also a source of organic arsenic). Other community members may have had similar interpretations of this guidance.

It is difficult to estimate dietary exposure to arsenic in environmental health investigations. International published studies examining levels of total arsenic in food

have ten fold or greater differences in the same food item. Examples include milk and cheese (0.003 ppm (LeBlancet al. 2005) to 0.039 ppm (Sapunar-Postruznik et al. 1996)), chicken (0.022 (LeBlanc et al. 2005) to 0.39 ppm (Lasky et al. 2004)), rice (0.005 to 0.710 ppm (Zavala and Duxbury 2008)) and green versus black tea (0.11 and 5.61 ppm respectively (Shen and Chen 2008)). The Food and Drug Administration (FDA) in the US has monitored arsenic in the Total Diet Survey for many years. The levels of arsenic intake have dropped across all food categories as a result of the legislation against using arsenic-containing pesticides on food crops (Jetliner and Cornelius 1977).

Studies focusing on the speciation of arsenic within food conclude that most of the arsenic is in the organic forms that are considered to be non-toxic to humans (ATSDR 2007). However, 67-90% of the arsenic in rice may be inorganic (Hamano-Nagoya et al. 2008; Mandal et al. 2007). The inorganic proportion in fish and seafood varies from 1-10% (ATSDR 2007). This variation in estimates of inorganic arsenic in food makes it difficult to estimate total dietary exposure to inorganic arsenic, with resultant difficulties in legislating acceptable limits in food. Australia is currently the only country which has established a maximum permitted concentration of 1 ppm in food (New South Wales Health Department 2001). The World Health Organization (WHO) and the US set provisional tolerable daily intake limits (PTDI) of 2.14 ug/kg bw/day (ATSDR 2007; Health Canada 2009). The values calculated by the investigative team for the risk posed by consumption of Restaurant A's fish and chips were well below the PTDI set by the WHO (Health Canada 2009).

As heavy metals test results for community members are not reportable to public health the exact numerator and denominator of those tested in Blackville may never be known. Contrast this with the residents' water sample results which were automatically copied to the local public health authorities. The monitoring of heavy metal toxicity and /or exposure risk factors is under consideration by Health Canada.

Recognition of potential population environmental exposures is therefore wholly reliant upon communication between clinicians and public health. Proactive surveillance of environmental health issues is a nascent public health phenomenon that would enable analysis of exposure and disease trends, allow early recognition and control of disease and evaluation of mitigation strategies for environmental hazards. The US Centers for Disease Control and Prevention has initiated the Environmental Public Health Tracking Program to follow hazards, exposures, biomonitoring and health effects (McGeehin 2004). Integrated environmental public health surveillance is also under development in Canada (Health Canada 2004), however, there are currently no reportable intoxications.

Conclusions

Field Epidemiologists were asked to assist in an investigation after four individuals with elevated blood arsenic were discovered in Blackville, NB. With the possible exception of the index individual whose diagnostic investigation continues, no evidence of arsenic toxicity was found among any community members tested and whose results were reviewed by the investigative team. The investigative team concluded that arsenic does not pose a threat to this community.

Recommendations

- Case validation of persons under investigation depended on a diagnostic test rarely used by physicians
 in the community. Reporting of specialized laboratory tests such as arsenic could be accompanied by
 guidelines for interpretation and recommendations about further testing. This would parallel the current
 system in New Brunswick for reporting of renal function tests, which are accompanied by an explanation
 of limitations of interpretation and suggestions for further testing.
- There is limited population level data for arsenic biomonitoring in Canada. Interpretation of biomonitoring is based on toxicology studies and population norms from the US, or populations tested by individual labs in order to establish their norms. These populations are not necessarily representative of Canadians. Continued participation from the Moncton region in the Canadian Health Measures Survey will help to rectify this data gap and provide a more suitable basis for comparison of arsenic testing in environmental investigations. This would be particularly useful in a province with a large mining and resource extraction sector.
- It is common practice for environmental investigations to examine geospatial distribution of cases. In this investigation we worked with local public health to overlay maps of cases' residences and environmental data (e.g., water testing). Access to professional expertise in GIS mapping at the local, provincial or federal level would have enhanced our spatial data analysis.
- In this investigation, community concern led to early and active political involvement at the local and provincial levels. The volatility of the situation was amplified by community allegations of withholding information sparked by laboratory delays. Environmental investigations with media/political attention would benefit from including person(s) with formal training in risk communication on the investigative team.
- Public health practitioners have limited access to professional development opportunities featuring
 environmental health investigation and/or risk communication. PHAC is supporting development of both
 on-line (Skills Enhancement) and interactive classroom modules (CFEP); course offerings in environmental
 health are planned for the future.

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Appendices

Background

- A. Inorganic and Organic Arsenic Speciation
- B. Symptoms Associated with Chronic Inorganic Arsenic Toxicity

Methods

- C. Algorithm for Public Health Investigation of Elevated Arsenic Levels Amongst Residents of a New Brunswick Community
- D. Medical History Questionnaire
- E. Factors that Affect Individual Responses to Arsenic Exposure
- F. Arsenic Case Finding Letter to Blackville Area Physicians
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- H. Metabolic Pathway for Inorganic Arsenic in Humans
- I. Number of Blackville Village Residents Submitting Specimens for Arsenic Testing by Specimen Type, November 2008 to February 2009
- J. Standardized Mortality Ratios (SMR) using Provincial Norms for Select Diseases and All Causes of Death for Blackville Village Residents, 2002-2006
- K. Map of Blackville Village Detailing Areas of Possible Historical Arsenic Sources, New Brunswick
- L. Spot Map of Private Wells in Blackville Village Tested for Arsenic in November 2008, New Brunswick
- M. Arsenic Content of Ground Water in New Brunswick, 1994-2008
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Discussion

- O. Comparison of Biomonitoring Results in Unexposed Populations and the Blackville Village Community Sampling November 2008 to February 2009, (n=63)
- P. Age Standardized Incidence Rates per 100,000 Population for Lung Cancer by Health Region and Gender, New Brunswick, 1999-2003
- Q. Persons and Organizations Contacted as Part of the Environmental Investigation

Appendix A: Inorganic and Organic Arsenic Speciation

Toxic, naturally occuring arsenic species OH OH HO—As HO—As = O OH OH Arsenic III Arsenic V Metabolic byproducts of arsenic V CH₃ CH₃ O = As — O O = As = O OH CH₃ Monomethyl arsenic Dimethyl arsine Nontoxic species of arsenic in food supply CH₃ CH₃ CH₃ CH₃ CH₃ CH₃ CH₃ CH₃ CH₂COH CH₃ CH₃ CH₃ CH₃ Arsenocholine Arsenobetaine

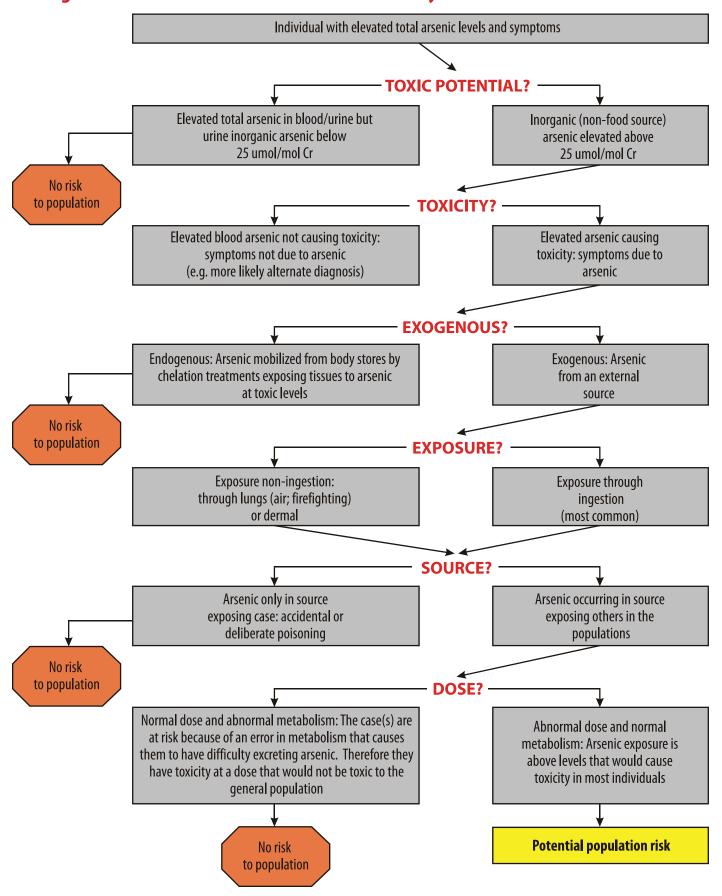
Source: SOS-Arsenic website

Appendix B: Symptoms Associated with Chronic Inorganic Arsenic Toxicity

Symptom/Disease	References
Cancers	IARC: carcinogen: group 1 EPA: cancer classification: group A Co-carcinogen w UV light and PAHs
Skin cancer: Squamous cell carcinoma (CC), Bowen's disease, Basal CC, combined skin cancer	Mead 2005, ATSDR 2007, Hall 2002
Liver cancer	Mead 2005, ATSDR 2007
Kidney and Bladder cancers (transitional CC of bladder)	Mead 2005, ATSDR 2007
Prostate	ATSDR 2007
Lung cancer (with inhalation and ingestion)	Mead 2005, ATSDR 2007
Myelogenous leukemia, Hodgkin's disease	Hall 2002
Respiratory	
Sore throat and irritated lungs (with inhalation of As)	ATSDR 2007
Decreased lung function (by spirometry)	ATSDR 2007
Bronchitis, Bronchiectasis, Bronchopneumonia	ATSDR 2007
Cardiovascular	
Atherosclerosis, thickening and vascular occlusion of blood vessels	Mead 2005, ATSDR 2007
Hypertension	Mead 2005
Gangrene of the feet "Blackfoot disease" (Taiwan)	Hall 2002
Reynaud's, Acrocyanosis	ATSDR 2007
Prolonged QT interval and Toursades de Pointes (with As trioxide used in tx of acute promyelocytic leukemia)	ATSDR 2007
Ischemic heart disease	ATSDR 2007
Blood and Lymphatics	
Anemia	Mead 2005, ATSDR
Pancytopenia	Mead 2005, ATSDR
Leukopenia	Mead 2005, ATSDR
Gastrointestinal	
Liver disorders	Mead 2005
Non-cirrhotic portal hypertension with bleeding esophageal varices, Splenomegaly, Hypersplenism – in those taking Fowler's solution	Nevens et al .1990 in Hall 2002
Nausea, Vomiting, Diarrhea, Abdominal pain	ATSDR 2007

Symptom/Disease	References
Renal	
Kidney dysfunction (with ingestion of methyl As in animals)	Mead 2005 ATSDR 2007
Bladder damage (with ingestion of methyl As in animals)	ATSDR 2007
Endocrine	
Diabetes mellitus	Mead 2005
Neurological	
Peripheral sensory neuropathy	Mead 2005, Hall 2002
Peripheral motor neuropathy: wrist drop, foot drop, altered reflexes; histology findings: dying-back axonopathy and demyelination	Mead 2005, Hall 2002, ATSDR 2007
Asymmetric bilateral phrenic neuropathy	Bansal et al. 1991 in Hall 2002
Headache	Mead 2005
Confusion and cognitive impairment	Mead 2005
Encephalopathy	Mead 2005
Dermatological	
Hyperkeratotic lesions ("wart-like")	Mead 2005, ATSDR 2007
Hyperkeratosis of the skin (palms and soles)	ATSDR 2007
Hyper- or hypo-pigmentation	Mead 2005, ATSDR 2007
Mees lines (transverse white lines on nails)	Hall 2002
Specific effects in children and reproduction	
Cognitive impairment (reduced IQ)	ATSDR 2007
Possible neurobehavioral disorders	ATSDR 2007
Increased mortality in young adults with exposure during gestation and early childhood	ATSDR 2007
Low birth weight, Fetal malformation, Fetal death (stillbirth, miscarriage), Preterm birth: animal studies, high inorganic As dose	ATSDR 2007

Appendix C: Algorithm for Public Health Investigation of Elevated Arsenic Levels Amongst Residents of a New Brunswick Community



Appendix D: Medical History Questionnaire

- What was the very first symptom that you felt? When?

Medical	ation into Elevated Blood Questionnaire - Generic N 1: 07 December 2008	Arsenic Levels	Case # : Date of Interview
- Purp natu - Over - All as This	ON duce self ose of the interview: to understand the sym ropathic treatments in order to better under all goal: identify risks to you and your comm spects are confidential and we will maintain information will not be shared with anyone of	rstand the links between you nunity due to arsenic exposu written and computer record	r illness and arsenic. re and to mitigate those risks. ds under the strictest confidentiality.
Record Start 1	ime of Interview:		
Age	Gender		
Street Addres	s	Postal Code	
SYMPTOMS			
Tell me about - If symptoma	your health: atic, then take specific history of the symptor	ms.	
Symptom	Describe the symptom. Onset, Duration, Severity, Current Status, other Comments	What did you do about the sought, effects of treatmen	
- When was *	he last time that you felt completely well?		

We will now ask you about all sorts of symptoms that you may have experienced.

Ask patient if they have ever had any of the following symptoms/illnesses: (skip/quickly review those that have already mentioned)

Symptom	Y/N and if Y then details (description, onset, duration, body site, treatments etc)	
Dermatological		
Hyperkeratotic lesions ("wart-like", corns)		
Hyperkeratosis ("thickening") of the skin (palms and soles)		
Light or dark skin patches (Hyper- or hypopigmentation) On: eyelids, intertriginous zones, areas of friction		
Rash		
Mees lines (transverse white lines on nails)		
Facial swelling		
*TAKE A PICTURE if possible		
Have you ever been told that you have cancer?		
Skin cancer: Squamous cell carcinoma, Basal CC, Bowens disease, combined skin cancers		
Liver cancer		
Kidney & Bladder cancers (transitional CC of bladder)		
Prostate Cancer		

	,
Lung cancer (with inhalation, and ingestion)	
Myelogenous leukemia	
Hodgkins disease	
Respiratory	
Sore throat & irritated lungs (on respiration of As)	
Asthma	
Decreased lung function (by spirometry)	
Bronchitis, Bronchiectasis, Bronchopneumonia	
Cardiovascular	
Atherosclerosis, thickening and vascular occlusion of blood vessels	
High blood pressure, Hypertension	
Heart attack, Angina, Ischemic heart disease	
Arrythmia, unusual heart rhythm. Prolonged QT interval and Toursades de Pointes (with As trioxide used in tx of acute promyelocytic leukemia)	
Gangrene of the feet "Blackfoot disease" (Taiwan)	
Raynauds, Acrocyanosis, coldness of hand/feet	

Acute: Myocarditis, Pericarditis	
Blood and Lymphatics	
Abnormalities of the blood	
Anemia (prompt: pernicious anemia)	
Pancytopenia	
Leukopenia	
Bone marrow failure	
Gastrointestinal	
Liver disorders (cirrhosis etc)	
Bleeding from the gut or vomiting blood [Non-cirrhotic portal hypertension w bleeding esophageal varices, splenomegaly, hypersplenism – in those taking Fowlers solution]	
Enlarged spleen	
Nausea, vomiting	
Diarrhea, Abdominal pain	
Acute: Metallic taste in mouth, (garlic odor, dyspepsia, severe jaundice)	
Renal	
Difficulty with urination: For example, not producing urine or having difficulty passing urine	

Blood in urine, or clumps of cells in bladder	
Painful urination (Dysuria)	
Kidney dysfunction [- w ingestion of methyl As in animals]	
Damage or disease of the bladder [tissue changes in animal model]	
Endocrine	
Diabetes mellitus	
Thyroid disease	
Neurological	
Loss of sensation in the hands or feet (Peripheral sensory neuropathy)	
Weakness or loss of movement in the hands or feet, arms or legs (Peripheral motor neuropathy: wrist drop, foot drop, altered reflexes)	
Weakness in breathing or inability to take a deep breath (Asymmetric bilateral phrenic neuropathy)	
Headache	
Confusion or difficulty thinking or concentrating (cognitive impairment)	
Back pain (firefighting)	

Changes in vision	
Changes in hearing	
Reproductive	Have you experienced the following symptoms in your reproductive years
A newborn with low birth weight (less than 5.5 lb)	
Miscarriage	
Still birth	
Pre-mature birth (i.e. before 36 weeks)	
The following symptoms in your children	
Difficulty learning	
Difficulty with social interactions	
Other: Allopecia (hair loss), apathy, salivation	

EFFECT OF SYMPTOMS ON FUNCTION

Throughout your illness:

Have your symptoms affected your ability to:

- Work? Please describe the details (which symptoms in particular, when, what activity limitations, any job changes duration, severity of limitation etc)
- **Volunteer? Please describe the details** (which symptoms in particular, when, what activity limitations, any job changes duration, severity of limitation etc)
- **Do chores around the house? Please describe the details** (when, what activity limitations, duration, severity of limitation etc)
- **Enjoy things like hobbies, recreation, time with family? Please describe** (when, what activity limitations, duration, severity of limitation etc)

PAST MEDICAL HISTORY

Please list all of your medical conditions

Diagnosis date,

Treatments in past and currently (including herbal, natural, diet...),

Current status (i.e. severity, worsening/stable/improving)

[many medical conditions were prompted above, no need to ask again if asked once]

Prompt: Nutrient deficiency? (e.g. cysteine, methionine, calcium, B-12, niacin (B3), choline)

Do you now or have you ever:

- Smoked?
 - o Cigarettes
 - roll you own:
 - pack- years,
 - date of quitting
- Pipes,
- Chewing tobacco (flavoured, source)
- Drink alcohol amount, duration, periods of drinking more than 3 drinks in one evening (looking for binge-drinking)
- Used marijuana (smoked, ingested)
- Hashish
- Heroin
- Cocaine snorted, smoked (crack cocaine)
- Crystal methamphetamine
- Any other recreational drugs of any kind (legal or illegal)

TREATMENT AND WORK UP FOR SUSPECTED AS TOXICITY OF SYMPTOMS OF UNKNOWN ETIOLOGY

Please list all physicians, specialists that you have seen and what tests they have done. Please do this to the best of your recollection. With your permission, we would also like to access your medical charts to collect the medical information

***collect consent if not already done so.

*** obtain any blood, urine or other results that patient has including tests for As but also, CBC, other blood tests etc

Prompts:

Family Doctor

Name

Contact Information (for all Family Physicians seen at regular clinic, walk-in clinic etc)

Date of first visit for symptoms:

Date of most recent visit for symptoms:

Type of care: once, episodic, on-going

For each symptom (if not listed above; If above, note the doctor beside the symptom)

- When visited,
- Nature of symptoms discussed
- Diagnoses given
- Any treatments (not mentioned above)
- Change of symptoms with treatment (improvement or deterioration and the specifics)

Specialists (Neurologist, Surgeon, etc)

- Name
- Contact Information

Date of first visit:

Date of most recent visit:

For each symptom (if not listed above; If above, note the doctor beside the symptom)

- When visited,

For each visit

- Nature of symptoms discussed
- Tests
- Diagnoses given
- Any treatments (not mentioned above)
- Change of symptoms with treatment (improvement or deterioration and the specifics)

Naturopath

- Name
- Contact Information

Date of first visit:

Date of most recent visit:

Type of care: once, episodic, on-going

For each symptom

- When visited, nature of symptoms discussed, diagnoses given, tests

Diagnoses given:

All treatments including calcium sodium EDTA, herbal, other remedies.

- Prompt: calendar, frequency of treatments

EDTA Treatment

Date	Treatment (dose, route, duration)	Comments (change in symptoms, other)

^{***} NOTE: the first date of chelation therapy is very important to obtain.

Any blood work done before the chelation therapy should be noted.

- Overall change of symptoms with treatment (improvement or deterioration and the specifics)

Other alternative or complementary medicine?

PROMPT: Homeopath, Chiropractic, Massage, Iridology, Reflexology

Name

Contact Information

Date of first visit for symptoms:

Date of most recent visit for symptoms:

Type of care: once, episodic, on-going

For each symptom (if not listed above; If above, note the doctor beside the symptom)

- When visited,
- Nature of symptoms discussed
- Diagnoses given
- Any treatments (not mentioned above)
- Change of symptoms with treatment (improvement or deterioration and the specifics)

Practitioner	Details

MEDICATIONS

Please list all medications that you have used since January 2005:

pills, liquids, natural remedies, herbal remedies, vitamins, ointments, creams, inhalation, incense, aromatherapy

Current

Start Date	Medication (list generic and company name)	Dose, Route, Frequency

Past (start and end date)

Start Date &End Date	Medication (list generic and company name)	Dose, Route, Frequency

Where do you get your medications? Including herbal, natural and those prescribed by a physician.

Is there any other aspect of your medical history that you would like to share with us? PROMPT: white forelock

Record time of interview completion:	
necold time of filterview completion.	

CONCLUSION

Thank you for your time. Information is confidential and will be used for public health the investigation of elevated arsenic levels.

If you would like to contact us, please call Miramichi Public Health at (506) 778-6765, and leave your name. We will return your call at the earliest convenience.

^{***}Obtain consent to access pharmaceutical records

Appendix E: Factors that Affect Individual Responses to Arsenic Exposure

Factors	References
Dose	
Duration of exposure	
Age	ATSDR 2007
Sex: Females have higher methylation efficiency than males	ATSDR 2007, Lindberg et al. 2007
Dietary	
Higher intakes of cysteine, methionine, calcium, protein, and vitamin B-12 were associated with lower percentages of inorganic arsenic and higher ratios of MMA to inorganic arsenic in urine. In addition, higher intakes of niacin and choline were associated with higher DMA/MMA ratios, after adjustment for sex, age, smoking, total urinary arsenic, and total energy intake	Heck et al. 2007, in ATSDR 2007 p.265
Iron, zinc, niacin: low dietary intake, higher MMA/DMA in urine	Steinmaus et al. 2005
Protein: low dietary intake, higher MMA/ DMA in urine	Steinmaus et al. 2005
Smoking: increases toxicity of As	ATSDR 2007
Icohol: increases toxicity of As	ATSDR 2007
Co-morbidities	ATSDR 2007

Appendix F: Arsenic Case Finding Letter to Blackville Area Physicians

December 8, 2008

To physicians practicing in Miramichi and serving patients from the Blackville area

Re: Testing for Arsenic in humans

Dear colleagues,

On the 14th of November, I wrote to you indicating that the Public Health office was aware of a couple of cases of individuals in the Blackville area found to have blood levels of arsenic higher than the norm. Since then, two more such cases have been found. The source of the arsenic intoxication is yet to be determined but two field epidemiologists from the Public Health Agency of Canada are currently assisting with the investigation since the 1st of December and we hope to have a breakthrough in the near future.

Low level arsenic exposure might eventually result in skin lesions, peripheral neuropathy, hypotension, cardiac arrhythmias, peripheral vasodilatation, congestive heart failure, anemia, abnormal liver function. Chronic low level arsenic exposure can also lead to various types of skin cancer and, in occupational settings, has been associated with lung cancer.

In the event that you see in your practice residents of Blackville with symptoms compatible with arsenic intoxication and wish to test them for arsenic, it is recommended that you order a first morning urine spot test for total arsenic, specifying on the requisition that the level of inorganic arsenic also be done if the total arsenic result is above 25 nmol/L. This test would best be performed after one week of dietary abstinence from seafood (including salmon). The urine arsenic test is preferable to the blood arsenic test, according to experts we have consulted.

Thank you in advance for your anticipated cooperation.

If you need more information, do not hesitate to contact my office.

Sincerely yours,

Denis G. Allard MD, MSc, FRCPC Regional Medical Officer of Health for Health Regions 1&7 P.O. Box 5001 81 Albert Street Moncton NB F1C 8R3

Appendix G: Hypothesis Generating Exposure Questionnaire

Investigation into Elevated Blood Arsenic Levels **Hypothesis Generating Questionnaire**

Good Afternoon, we are Field Epidemiologists and are part of the New Brunswick Department of Health Investigation Team. We are looking into reports of elevated blood levels of arsenic in residents of Blackville NB. We would like to ask you some questions regarding your health and your lifestyle as part of our investigation into

	e exposures to arsenic. This information e approximately two hours. If you do n		u give u		
	a break let me know.	Ot Wisii t	.0 4113	one or the qu	estions it is on to refuse. If you freed
	ew start	Intervie	ew Finish	າ	
Case #	graphics Age Gender How long have you lived in Blackville? Where did you live before moving to E				
Occupa	ation				
3. 3a 3b	Have you or do you worked for any of Armed Forces Saw Mill Cotton fields/orchards Mining If Yes, please specify Where was this?	☐ Glass /Smeltin	Industr ig (esp co	opper, lead, cobo	alt, gold, zińc, silver)
	t Employer				
4. 5.	Current place of employment How long have you worked there?				
5. 6.	Briefly describe your job				
7.	Has your job description changed ove	r the vea	ars. 🗆 Y	es □No □	Can't recall
	If Yes 7a Why?				
8.	What is the water source at work? W	/ell □ M	unicipal	water 🖵 Bottle	ed water 🖵 Unknown
9.	Do you drink from the tap?	□ No □	⊒ Unkno	own 🚨 Can't re	call
	If Yes	-•			
10	9a. please specify □ Rarely □ Sc				
10.	How much water do you drink at w				
11.	☐ Less then one cup day ☐ 1-2 cu Have you noticed strong or strange of				
11.	If yes please specify:	וו מוסג	ie work	Jiace: 🗖 Tes 📮	NO Carrenecali
11a.	What kind of odor?				
11b.	When did this occur?				
11c.	How many times?				
11d.	Who else was exposed?				
12.	Do you work with?				
	•				☐ Can't recall
	Lab/Chemical reagents	☐ Yes	□ No	☐ Unknown	☐ Can't recall
	Chemical fertilizer	☐ Yes	□ No	☐ Unknown	☐ Can't recall
	Pesticides Pat poison	☐ Yes	□ No □ No	☐ Unknown	☐ Can't recall☐ Cant' recall☐
	Rat poison Paints/thinners/solvents	☐ Yes☐ Yes	□ No	☐ Unknown☐ Unknown	☐ Can't recall
	Fowlers solution, Paris green paint	☐ Yes	☐ No	Unknown	☐ Can't recall
	Agricultural chemicals	☐ Yes	☐ No	☐ Unknown	☐ Can't recall
	Feed production	☐ Yes	□No	☐ Unknown	☐ Can't recall
If Yes to	any of the above, please elaborate		-		
12a.	Name/brand name of item				
12b.	When?				
12c.	Where?				

13. 14.	In this job, approximately how Do you work with /chemically recall							
14a.	If yes specify type of wood tre	atment						
15.	Do you build structures/ prod	ucts using	nressi	re treated/che	mically t	reated w	vood?	
15.	☐ Yes ☐ No ☐ Unknown	Can't	recall	ire treated, erre	inically c	catea v	vood.	
16.	Have you been exposed to the							
				□ Unknown				
	Scrap lumber Plywood	☐ Yes	□ No	Unknown				
	Creosote treated wood	□ Yes	□ No	Unknown				
	(ie fence posts, railway ties, el							
	If Yes, specify if 16a . the wood			treated or pain	nted			
17. Wh	at type of fire was it? (i.e. struc							
	71	,		,				
Previo	us Employer							
18.	Previous place of employment	t						
19 .	Previous job description							
20.	How long did you work there?	<u> </u>						
21.	When did you change Jobs?							
22 .	Why did you change jobs?							
	☐ Better employment opport	unity						
	☐ Health condition							
	Other please specify							
23 .	What was the water source at	your prev	ious wo	orkplace?				
	☐ Well ☐ Municipal water	☐ Bottle	ed wate	er	Unki	nown	Can't recall	
24.	Did you drink from the tap? If Yes please specify	☐ Yes	ı	No UUni	known	☐ Can'	t recall	
24a.	If yes please specify	Rareı 🎞	y 	Sometime	'S	☐ AIW	ays	((()
25.	How much water did you di							
26.	Less then one cup day Did you ever notice strong							ay
20.	Did you ever notice strong of				ious wo	кріасе	:	
26-	☐ Yes ☐ No ☐ Can't Recall							
26a. 26b.	What kind of odor?							
ZOU.								
	When did this occur?							
26c.	How many times?							
26c. 26d.	Who else was exposed,?							
26c.	Who else was exposed,? Did you work with any of the f	ollowing	?					
26c. 26d.	Who else was exposed,? Did you work with any of the f Wood preservatives	ollowing	? □ No	□ Unknown	☐ Can't	recall		
26c. 26d.	Who else was exposed,? Did you work with any of the f Wood preservatives Lab/Chemical reagents	ollowing Yes Yes	? □ No □ No	□ Unknown	□ Can't	recall recall		
26c. 26d.	Who else was exposed,? Did you work with any of the f Wood preservatives Lab/Chemical reagents Chemical fertilizer	ollowing Yes Yes Yes	? No No	□ Unknown □ Unknown □ Unknown	□ Can't □ Can't □ Can't	recall recall recall		
26c. 26d.	Who else was exposed,? Did you work with any of the f Wood preservatives Lab/Chemical reagents Chemical fertilizer Pesticides	following: Yes Yes Yes Yes Yes	P No No No	□ Unknown □ Unknown □ Unknown □ Unknown	□ Can't □ Can't □ Can't □ Can't	recall recall recall recall		
26c. 26d.	Who else was exposed,? Did you work with any of the f Wood preservatives Lab/Chemical reagents Chemical fertilizer	ollowing Yes Yes Yes Yes Yes Yes Yes	P No No No No	□ Unknown □ Unknown □ Unknown □ Unknown □ Unknown	Can't Can't Can't Can't Can't Can't	recall recall recall recall recall		
26c. 26d.	Who else was exposed,? Did you work with any of the f Wood preservatives Lab/Chemical reagents Chemical fertilizer Pesticides Rat poison	ollowing Yes Yes Yes Yes Yes Yes Yes	P No No No No No	□ Unknown □ Unknown □ Unknown □ Unknown	□ Can't	recall recall recall recall recall recall		
26c. 26d.	Who else was exposed,? Did you work with any of the f Wood preservatives Lab/Chemical reagents Chemical fertilizer Pesticides Rat poison Paints/thinners/solvents Fowlers solution	ollowing Yes Yes Yes Yes Yes Yes Yes	P No No No No No No No	□ Unknown □ Unknown □ Unknown □ Unknown □ Unknown □ Unknown	□ Can't	recall recall recall recall recall recall recall		
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26c. 26d.	Who else was exposed,? Did you work with any of the f Wood preservatives Lab/Chemical reagents Chemical fertilizer Pesticides Rat poison Paints/thinners/solvents Fowlers solution Paris green paint	ollowing Yes	P No No No No No No No No No	□ Unknown	□ Can't	recall recall recall recall recall recall recall recall		
26c. 26d.	Who else was exposed,? Did you work with any of the f Wood preservatives Lab/Chemical reagents Chemical fertilizer Pesticides Rat poison Paints/thinners/solvents Fowlers solution Paris green paint Agricultural chemicals Feed production If Yes to any of the above pleas	ollowing Yes Yes Yes Yes Yes Yes Yes Yes Yes Ye	P No	Unknown	□ Can't	recall recall recall recall recall recall recall recall recall		
26c. 26d.	Who else was exposed,? Did you work with any of the f Wood preservatives Lab/Chemical reagents Chemical fertilizer Pesticides Rat poison Paints/thinners/solvents Fowlers solution Paris green paint Agricultural chemicals Feed production If Yes to any of the above pleas	ollowing Yes Yes Yes Yes Yes Yes Yes Yes Yes Ye	P No	Unknown	□ Can't	recall recall recall recall recall recall recall recall recall		
26c. 26d. 27.	Who else was exposed,? Did you work with any of the f Wood preservatives Lab/Chemical reagents Chemical fertilizer Pesticides Rat poison Paints/thinners/solvents Fowlers solution Paris green paint Agricultural chemicals Feed production If Yes to any of the above pleas Name/brand name of item When?	ollowing: Yes Yes Yes Yes Yes Yes Yes Yes Yes Ye	P No	Unknown	□ Can't	recall recall recall recall recall recall recall recall recall		
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26c. 26d. 27. 27a. 27b. 27c. 27d. 28.	Who else was exposed,? Did you work with any of the f Wood preservatives Lab/Chemical reagents Chemical fertilizer Pesticides Rat poison Paints/thinners/solvents Fowlers solution Paris green paint Agricultural chemicals Feed production If Yes to any of the above pleas Name/brand name of item When? Where? In this job, approximately how Did you work with /chemically □ Yes □ No □ Unknown If yes specify type of wood tre Did you build structures/ prod □ Yes □ No □ Unknown Were you been exposed to the	ollowing: Yes Can't atment _ lucts usin Can't eburning	P No Tecall of?	Unknown	Can't	recall recall recall recall recall recall recall recall recall	 ove products? _	
26c. 26d. 27. 27a. 27b. 27c. 27d. 28a. 29.	Who else was exposed,? Did you work with any of the f Wood preservatives Lab/Chemical reagents Chemical fertilizer Pesticides Rat poison Paints/thinners/solvents Fowlers solution Paris green paint Agricultural chemicals Feed production If Yes to any of the above pleas Name/brand name of item When? Where? In this job, approximately how Did you work with /chemically Yes No Unknown If yes specify type of wood tre Did you build structures/ prod Yes No Unknown Were you been exposed to the Scrap lumber	ollowing: Yes Can't Can't burning Yes	P No ate	Unknown	Can't	recall recall recall recall recall recall recall recall recall	 ove products? _	
26c. 26d. 27. 27a. 27b. 27c. 27d. 28a. 29.	Who else was exposed,? Did you work with any of the f Wood preservatives Lab/Chemical reagents Chemical fertilizer Pesticides Rat poison Paints/thinners/solvents Fowlers solution Paris green paint Agricultural chemicals Feed production If Yes to any of the above pleas Name/brand name of item When? Where? In this job, approximately how Did you work with /chemically □ Yes □ No □ Unknown If yes specify type of wood tre Did you build structures/ prod □ Yes □ No □ Unknown Were you been exposed to the	ollowing: Yes Can't Can't burning Yes	P No recall g press recall of?	Unknown	Can't	recall recall recall recall recall recall recall recall recall	 ove products? _	

(ie fen 30a.	ce posts, railway ties, elec If Yes, specify if the wo			ated or na	inted			
31.	What type of fire was i							
32.	Do you have any medi						olaces?	
32a.	☐ Yes ☐ No ☐ Unk							
32b.	Nature of health conce When did you notice of	hange in yo	ur health?					
		,						
Hobbi 33.	DI III III	ac.						
34.	Do you have any hobb	ies or "side i	obs" that i	nvolved:	(i.e help	ing a friend, vo	olunteerina.)	
.	Furniture stripping	,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,	oos maci			☐ Unknown	runteening,,	
	Sand blasting			☐ Yes	■ No	■ Unknown		
	Insulation or manufact	ture of ureth	ane foam	☐ Yes	□ No	■ Unknown		
	Manufacture of furnitu	ire /woodwo	rking	Yes	□ No	■ Unknown		
	Paints					Unknown		
	Antifouling paint (ie m	narine paint)				Unknown		
	Solvents					Unknown		
	Ceramics					☐ Unknown		
	Glazes					☐ Unknown		
	Ball bearings					Unknown		
	Lead acid batteries					Unknown		
	Building/repairing elec	ctrical equip	ment			☐ Unknown		
	Semi conductors					☐ Unknown		
	Computer chips Solar panels					☐ Unknown☐ Unknown		
	Joiai parieis			— 163		- OHRHOWH		
Volunt	teer work							
35.	Please list any volunte	er activities						
F: 40 £ 6	htous							
<u>Fire fig</u> 36.		vou a fire fie	htor?					
30. 37.	How many years were Were you ever expose							
37.	Fire retardants	u to the folic		known	☐ Can	t rocall		
	Smoke inhalation							
	Burning cars/trucks							
	Burning solar panels	☐ Yes ☐	No □Ur	known		t recall		
	Burning buildings					t recall		
	Residential	☐ Yes ☐		known		t recall		
	Barns	☐ Yes ☐		nknown		t recall		
	Storage sheds	☐ Yes ☐	No 🖵 Ur	nknown	☐ Can	t recall		
	Industrial sites	☐ Yes ☐	No 🖵 Ur	nknown	☐ Can	't recall		
	Manufacturing sites	☐ Yes ☐		nknown	Can	t recall		
	Chemical factories	☐ Yes ☐		nknown		t recall		
	Fertilizer plants	☐ Yes ☐		nknown		't recall		
	Lumber yard	☐ Yes ☐		known		t recall		
	Wood fires	☐ Yes ☐	No 🖵 Ur	ıknown	□ Can	t recall		
38.	What type of wood str	ucture was l	ourned? i.	e. decking	, woodei	n fencing, scrap	lumber pile, lun	nber yard
	5 1 1 (5)							5 . (5)
	Description of Fire				wearing	g of personal	Time spent at Fire	Date of Fire
					protect		1116	
	you suffer any ill effects	s from any fi	re? 🖵 Ye	s 🖵 No	☐ Unk	nown 🖵 Ca	n't recall	
	Yes specify							
40. We	re you hospitalized? Yes specify	☐ Yes ☐	No 🖵 Ur	ıknown				

Sports 41. Please list all sports activities you are involved in currently and in the past

Huntir	ng and Fishin	q									
42.	Do you hunt		□No □U	nknown							
43.					se/aee	se/birds	□ Othe	er specif	v		
44.								☐ 1-2 times in past 5 years			_
		,		ot for 10 yea		,	,		as a chil		
45.	Do you eat v	vild meat?				Can't re	call	,			
45a.	If Yes please	specify spe	cies —								
46.	Do you hunt	for winter i	orovisions?	□ Yes	\square No	□ Unk	nown				
47 .	Do you freez	re meat	510 11310113.	□ Yes		□Unk	nown				
48 .	Dry meat	.c meat		☐ Yes		□Unk	nown				
49.	Smoke meat			☐ Yes		□ Unk	nown				
50.	Do you have	anv sample	25	☐ Yes							
51.	Have you ev	er done (fo	r vourself or i	for others)		_ 0					
J 1.	Tanning hide		yoursen or i	☐ Yes	□ No	□Unk	nown				
	Taxidermy			☐ Yes							
52 .	Do you make	e vour own	ammunition	n? □Yes		□Unk	nown	☐ Can'	t recall		
52a	16 Va a la a 4 a										
52b	If Yes, what a Do you still h Do you fish? Where do yo	nave samnle	.c7	□ Yes		□Unk	nown				
53.	Do you fish?	iave sample	-3.	☐ Yes		□Unk	nown	□ Can'	t recall		
54.	Where do yo	u fish?		— 163	_ o	— OIII	IIIOVVII	- Carr	Ciccan		
55.	Where do yo How often d	o vou fish?	□ Year roun	d Dlesst	han 5	times ne	er vear	☐ Fver	v few vez	arc	
<i>JJ</i> .	now orten a	o you nism.	☐ More the	n 10 vears a	חר	times pe	i yeai		child onl	V	
56 .	What type of			i io years a	90			- 7.5 a	Cilia oili	У	
50 .	□Haddock			le □ Plaice	.		□Sardi	nes	□Smelt	□Sal	lmon
	L indudock			ic Trialec	•		— 5arar	1103	<u> a</u> sincio	 5ai	
	☐Trout ☐ (Cod	□ Gasperea	ux 🖵 Shad	□ Stri	pped	☐ Bass		☐ Lobst	ter 🖵 Cr	ab
	☐ Shellfish				,	-					00
57.	Do you eat t			☐ Yes	□ No	□ Unk	nown	□ Can'	t recall		
	If Yes 57a .Do	o vou stock	vour freeze	with fish?		☐ Yes	□ No	□ Unk	nown		
57b.	Do you have	samples?	,	□ Yes	□ No	□Unk	nown				
58 .	Do you have How much v	vild fish do	vou consum	e? 🔲 2-3 ti	mes /v	veek	☐ Onc	e a weel	⟨ 🗖 2-3 ti	mes/month	
			,	☐ Once	a mor	nth	Less	than or	ice/mont	h	
59 .Wh	en was your la	ast wild fish	meal?	_ 0ee	uo.			triair or	,		
	, , , , , , , , , , , , , , , , , , , ,										
Housir	na										
	Are you curr	ently livina	in:								
	☐ Own Hous			wn Apartm	ent	□ Ren	tal Apart	ment	☐ Othe	r	
61.	Number of p									•	
62 .	When was th		_								
63 .	How long ha										
64.	Where did yo										
65.	Does your ho				□ Yes	□ No					
66.	What are the						most of	the time	in?		
.	Wildt are the	types of he	Joi covering	15 111 1110 100	iiis yo	азрена	111036 01	circ cirric			
					1		1		1		
Room	,	Wood	Vinyl	Carpet	Cor	crete	Tile	Othe	ar	Year	
Noon	1	vvood	VIIIYI	Carpet	Coi	iciete	1116	Oth	ΞI	installed	
										ilistalled	
- I											
Bedro	om										
Kitche											
KITCH	C11						1				
Famil	y room										
	•			+	_		+	+			

Othe	r specify									
67. 68. 69.	What are the When was th Have you car Yes No The type of re	rie last time y ried out any Unkno enovation _	vou redecora v major struc own □ Ca	ated? ctural reno n't recall	vations If Yes p	to your please sp	home? pecify:			
69b.	Date Did you do se		C 4 la a a l . 2							
69c. 69d.	Did you do so Did you wear	ome or all o	o mack?	☐ Yes		Unk	nown			
69a.	Did you wear							□Unknown		
OJE.	If yes, explain					— 163	_ 110	- OTIKITOWIT		
70 .	What is the h	neating sour	ce in vour ho	ome?	□ Oil f	urnace	☐ Gas f	urnace	_	
2 0.	☐ Electricity									
								☐ Other <i>please</i>	specify	
	-1 (J	3,						,	
	If yes to woo	d stove spec	ify:							
70a.	What type of									
70b .	Is it treated v									
71 .	Do you use a	ny kind of a	ir/heat exch	ange syste	em?	Yes	☐ No	Unknown		
72 .	Do you have	or use any k	kind of air filt	tration?		☐ Yes	☐ No	□ Unknown		
	If yes, please Do you use a	specify								
73 .	Do you use a	iny type of h	umidifier?	□ Yes	□ No	□ Unk	nown			
7.4	If Yes, please Do you have	specify								
74 .	Do you nave	an air nitrat	ion system?	□ Yes	□ NO	□ Unk	nown			
75	If Yes, please Do you have	specify		-2 D Vac	□ Na					
75 .	If you whore	any moula	ın your nom	e: u res	□ NO	□ Unk	nown			
76.	Have you had	d vour house	e sprayed fo	r nacts su	h as an	ts roach	ac flasc	ticks, rodents e	tc?	
70.	☐ Yes ☐ No	u your nous	wn If ves	specify	45 41	ts, roaci	ics, ricas,	ticks, roaciits c	····	
76 a.	What produc									
76b.	When?									
76 c.	How often?_									
76d.	By whom?								_	
76e.	Were you at I	home? 👢	lYes □ No	🖵 Unki	nown					
77 .										
77a.	Do you give									
78 .						al feed a	nt killer,	weed killer, rat p	ooison, in yo	our home
	or yard?		⊒Yes □ No		nown					
78a.	If yes, specify									
78b.	How long ha						ll'	,		
79.	Do you know				on in th	e neight	ornood	<i>:</i>		
79a	☐ Yes ☐ No			specify						
79a 79b.	Where,									
79c.	When									
/ JC.	What									
Home	Water Source	<u>.</u>								
80.	What is the n		ource for vo	ur home?						
	☐ Private we				ater					
	☐ Surface wa		Bottled wa		☐ Oth	er				
80a.					oottled	water				
80b.										
81 .	Frequencies									
	□ >10 glasse	es/day	1 5-10 glass€	es/day		glasses/o	day			
82 .	Do you drink				☐ Yes		Ŭ No			
83 .	Do you cook						☐ No		nown	
84 .			nost of the ti			water		ed Water		

	(please specify)
85.	(please specify) When was the last time the water was tested?
86 .	what was tested for? \square Bacteria \square Inordanics \square Other
87 .	Has it ever been tested for arsenic? ☐ Yes ☐ No ☐ Unknown
87a.	If yes, what were the results?
88.	Do you allow your tap water to run for a few minutes before drinking? ☐ Yes ☐ No ☐ Unknown
89. 89a.	Do you use any kind of a water filter/distiller?
	,, p
Outdo	<u>ors</u>
90 .	Do you have an outdoor fire pit? ☐ Yes ☐ No ☐ Unknown
90a.	If Yes, what type of wood/fuel is burnt?
91.	Do you have a garden? ☐ Yes ☐ No
	☐ Flowers ☐ Vegetables ☐ Fruit ☐ Mixed
92 .	Do you eat vegetables/fruits from your garden?
	☐ Yes ☐ No ☐ Unknown If Yes, please specify
92a.	Name of produce
92b.	Name of produce Amount of produce consumed Time of year produce consumed
92c. 93.	Time of year produce consumed
93 . 93a.	Do you freeze produce for the winter?
93a. 94.	Are there any samples? Do you wear gardening gloves? Yes No Unknown
95.	Do you eat/drink during gardening?
96.	Do you use any of the following for your garden?
	Pesticides
	Fungicide
	Insecticide
	Manure ☐ Yes ☐ No ☐ Unknown
	Fertilizers
	Mulch (ie treated wood chips from local mill) ☐ Yes ☐ No ☐ Unknown
96a.	If Yes, please specify name
97 .	Do you wear personal protective stuff while applying above products?
98.	☐ Yes ☐ No ☐ Unknown ☐ Can't recall Do you have any wood construction on your property? ie decks, patios, raised flower beds, fence posts
90.	☐ Yes ☐ No 98a. If Yes please specify
98b.	Who built #2
98c.	Were you involved?
99.	Do you know what was here on your property before your house was built?
100.	Can you think of anywhere around your home where neighbors or industries may be using arsenic?
	☐ Yes ☐ No ☐ Unknown If yes, please specify
	ational Property
101.	Do you spend time at a Cabin/cottage/hunting camp? ☐ Yes ☐ No ☐ Unknown
100	If Yes 101a . Location of property Do you go there in? □ Spring □ Summer □ Fall □ Winter □ Year Round
102.	, 5
103.	How often do you go there? ☐ Every year ☐ Every few years ☐ Not in the past 5 years ☐ More than 10 years ago ☐ Other
104.	If you went this year, how often?
107.	Less than 3 weeks in total
105.	Water source at property ☐ Private well ☐ Shared well ☐ Municipal water
	□ Surface water □ Bottled water □ Other
105a.	
106.	When was the last time the water was tested?
107 .	What was tested for? ☐ Bacteria ☐ Inorganics ☐ Other
108.	Has it ever been tested for arsenic? ☐ Yes ☐ No ☐ Unknown
	Test result □ Oil furnace □ Gas furnace □ Electricity baseboard heaters
109	Heating source at property \square Oil furnace \square Gas furnace \square Flectricity baseboard heaters

	☐ Forced air ☐ Radiators ☐ Wood stove ☐ Fireplace ☐ Coal oil lamps ☐ Other please specify
109a. 110.	If Yes to wood stove please specify type of wood burnt Have you used pesticides, herbicides, insecticides or chemicals on this property? \(\subseteq \text{ No } \subseteq \text{ Unknown} \)
111. 111a.	
Vacati 112.	on/Travel Have you travelled outside of New Brunswick in the past 5 years? ☐ Yes ☐ No ☐ Can't recall If Yes,
112a. 112b.	Where
DIET 113 .	Has your diet changed significantly over the past few years? ☐ Yes ☐ No ☐ Unknown If yes, please specify:
113b.	Why did you make changes?What did you eliminate?
114.	What did you add? Did these changes affect your health?
115.	If yes please specify
	Supplements Kelp supplements Chinese medications i.e. Kushtay Shark cartilage Yes No Unknown Unknown Unknown Unknown Unknown Unknown
115a.	If Yes to the above products please specify
115c.	Name/typeHow long you have been taking themWhere do you buy them? (store ,internee, friend, doctor) Do you always buy the same brand or what is on sale?
116.	Are you currently taking (or in the past) any Homeopathic or Naturopathic supplements/medications/drinks/poultices/creams/drops? Yes No Unknown If yes please specify
116a.	Name/type How long have you been taking this
117.	Are you or have you been on any special dietary plan ie low protein, Yes No Unknown 117a. If Yes, please specify
<u>Food</u> 118 .	Where do you shop? □ Local grocery store □ Farmers Market □ Local produce stalls □ Other please specify □ Do you have any food allergies? □ Yes □ No □ Unknown
120.	If Yes please specify What foods do you not like?
120a. 121.	Do you avoid them or just eat smaller amounts?Are there any foods that you absolutely avoid?
121a.	Why do you avoid them?
122.	Is there any food item that you eat but others in your family do not eat? Yes No Unknown 122a If yes, please specify
123. 124.	Which restaurants/fast food places do you usually go to? How often do you go to these places?
125.	List general types of foods that you may consume on a regular basis . This should include foods consumed
	in the last few years and any beverages and snacks.

Breakfast	Snack	Lunch	Snack	Dinner	Snack

126. Do you or have you eaten any of the following foods?

Food item	Less than once a month	Once a month	Between once a month and once a week	More than once a week
Venison/beef				
Broiler chicken				
Store bought juices				
Dulse/seaweed/kelp				
Mushrooms, fresh				
Mushrooms, canned				
Mushrooms, bottled				
Mushrooms, dried				
Rice				
Rice bran/rice cakes				
Rice cakes/crackers				
Turnips				
Parsnips				
Carrots				
Potatoes				
Onions				
Specialty/Imported foods i.e.				
Candy				
Liquor				
Cakes/sweets				

Pickle	es							
Soft c	drinks							
127 A	pproximately how	much a	and what typ	e of sea	food do y	ou eat :		
Туре	Type of Seafood		N	o	Yes	How often		
Lobst	er							
Crab								
Shellf	fish (oyster, clams,	, mussel	s, scallops)					
Hadd	ock							
Sole								
Plaice	5							
Sardi	nes							
Smelt	t							
Tuna								
Salmo	on							
Trout								
Cod								
Gasp	ereax							
Shad								
Stripe	e Bass							
Othe	r specify							
128. 129. 129a. 129b. 130. 131.	B. Approximately how much beef do you eat per month? Do you eat organically grown foods? □ Yes □ No □ Unknown Where do you buy these foods? □ Same grocery store as other groceries market □ Other specify If yes please specify What products and how often? Do you routinely eat three meals a day? □ Yes □ No □ Unknown Do you eat at least three servings of fruits and vegetables a day? □ Yes □ No □ Unknown							☐ Farme
Drinks 133. 134. 134a. 135.	How much wate Do you regularly If yes specify bra What do you usu Breakfast Lunch Dinner Other	drink b nd and Ially drir	ottled water amount cons nk with meals	? • Yesumed s? (I.e. ju	ice, milk, o	coffee, wat	er, alcohol, soft drin	

137. 137a. 138. 138a. 138b.	Do you of What kind Whole Do you of Name of How man Do you re List other	Irink milk? Id of milk do milk 2% Irink alcohol drink ny drinks per ny years nake your ov	the name of the p Yes No you usually drink Skim milk ic beverages? week vn wine/beer? drink on a typical	Unknow? Soya mil Yes Yes	n k	Rice milk 「Jnknown If y	⊒_Other ves please ———	specify	
141. 141b. 142.	Are your Plastic Melam Where an Have you If Yes, spowhat is you	nine Ot re your dishe u made any d ecify Why your Cutlery	es manufactured? changes in dishes made of?	☐ Unknow lately? ☐ \	n ′es □1	No 🚨 Unkno		Can't recall	
144.	Metal	ess steel nade of the	\square Silve following and how	erware 🔲 F				□ Unknown	
Type o	of Pot &	Stainless steel	Teflon Coated	Copper	Iron	Aluminum	Other	Frequency of use	
Fry pa	n								
Large pot	Cooking								
Small	cooking								
Doubl	e boiler								
Griddl	e								
145. 145a. 146. 147. 148. 149. 149a. 150. 151. 152.	What made Do you use Do you use What type Self .(i.e. Do you collected from Clothes (i.e. Dishes (i.e. Other cleaners)	ide you to chase a microwase it every do e of productions soap, shamp coloring and Do your owner. Eabric softe, detergent, eaning products.	ay? ts do you use for voo, gel, body wash perm your hair? vn	washing? ple n) end does it f gent, glass cl	Yes IN Ye	No Unknownify No Beauty OS pads, scour	y salon? ring pads)_ s, furniture	cleaners/polishes, fl	oor

154. 154a.	Any recent changes in the products you use? What made you change products?	□Yes	□No	☐ Unknown				
154b. 155.	4b . Which products did you change?		□No	Unknown				
Anima	ls							
156 .	Do you have pets?	☐ Yes	■ No					
157 .	Do you give your pet treatments for ticks?	☐ Yes	□ No	□ Unknown				
158 .	Are you around farm animals?	Yes	■ No	■ Unknown				
159.	Have you handled medications/feed/horse liniment/anything the vets use? ☐ Yes ☐ No ☐ Unknown							
159a.	If yes, please specify what and when							
Other 160.	Is there anything else you want to tell me?							

Thank you for agreeing to participate in this interview. All your answers will be kept confidential. If you have any further questions or concerns please call Miramichi Public Health

Appendix H. Metabolic Pathway for Inorganic Arsenic in Humans

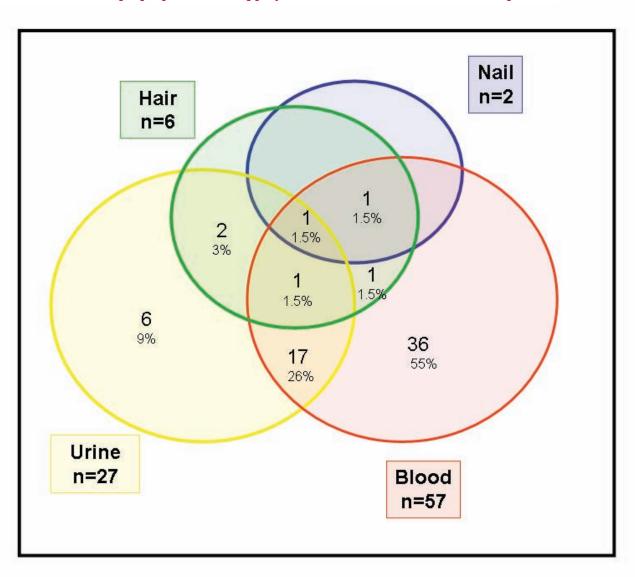
Inorganic arsenic

- -methylation --> monomethylarsonic acid (MMA 5)
- -reduction --> monomethyl arsonous acid (MMA3)
- -methylation --> dimethyl arsenic acid (DMA5)
- -reduction --> dimethylarinous acid (DMA3)

In humans the process is incomplete and general 10-20% is excreted as inorganic arsenic, 10-15% as monomethyl arsenic (MMA) and 60-75% as dimethyl arsenic

(DMA; Steinmaus et al. 2005).

Appendix I: Number of Blackville Village Residents (n=65)* Submitting Specimens for Arsenic Testing by Specimen Type, November 2008 to February 2009



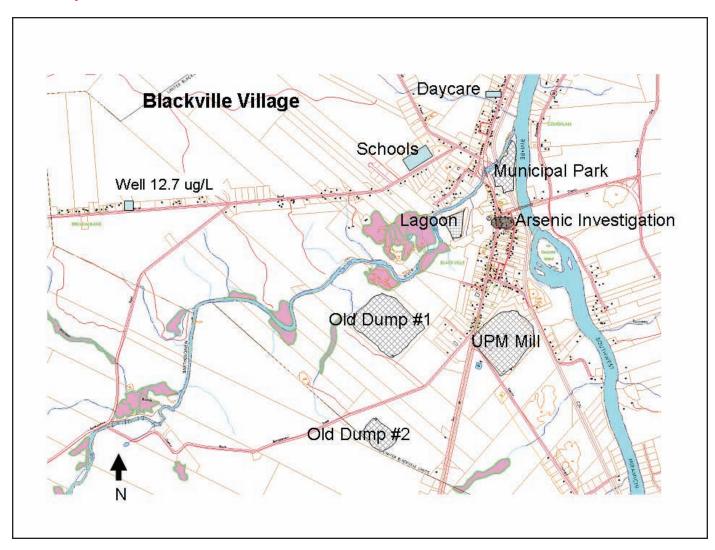
<sup>Excludes initial four persons under investigation
65 Blackville residents submitted a total of 92 specimens</sup>

Appendix J: Standardized Mortality Ratios (SMR) using Provincial Norms for Select Diseases and All Causes of Death for Blackville Village Residents, 2002-2006

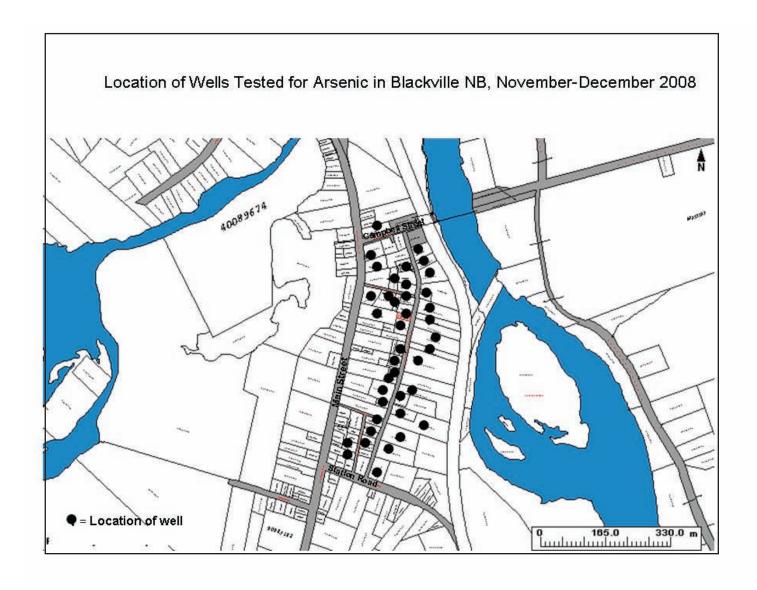
Males	Expected	Observed	SMR (lower C.I. to higher C.I.)
Lung cancer	1.8	X*	1.1 (-0.44 to 2.65)
All cancer	5.3	6	1.1 (0.22 to 2.04)
Kidney disease	0	0	0 (0 to 0)
Disease of circulatory system	8.9	X*	0.4 (0.01 to 0.89)
All causes of death	17.4	14	0.8 (0.38 to 1.23)
Females	Expected	Observed	SMR (lower C.I. to higher C.I.)
Lung cancer	1.5	5	3.3 (0.40 to 6.26)
All cancer	6.2	11	1.8 (0.72 to 2.81)
Kidney disease	0.6	X*	3.1 (-1.21 to 7.38)
Disease of circulatory system	5.4	X*	0.7 (0.01 to 1.48)
All causes of death	25.5	21	0.8 (0.47 to 1.18)

X* Actual number suppressed to meet confidentiality requirements Source: NB Vital Statistics

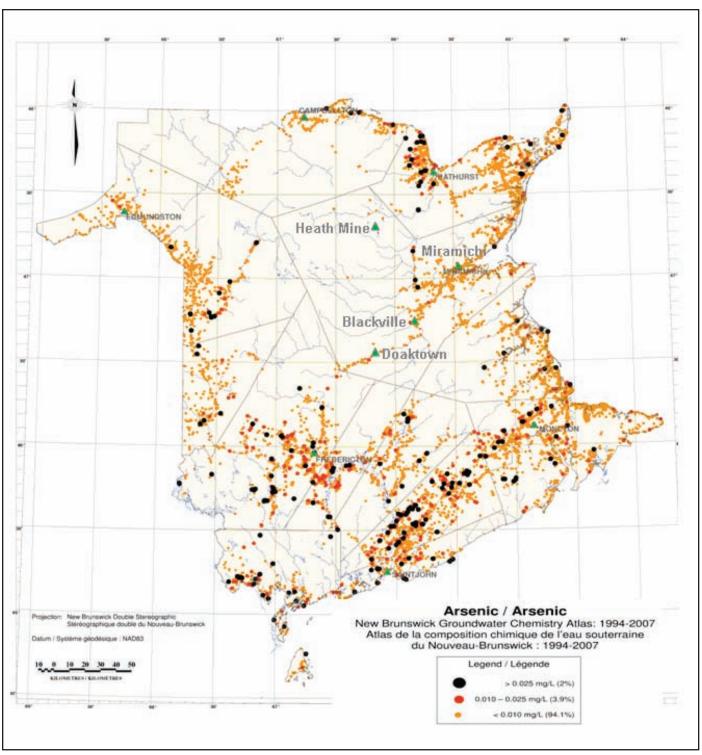
Appendix K: Map of Blackville Village Detailing Areas of Possible Historical Arsenic Sources, New Brunswick



Appendix L: Spot Map of Private Wells in Blackville Village Tested for Arsenic in November 2008, New Brunswick

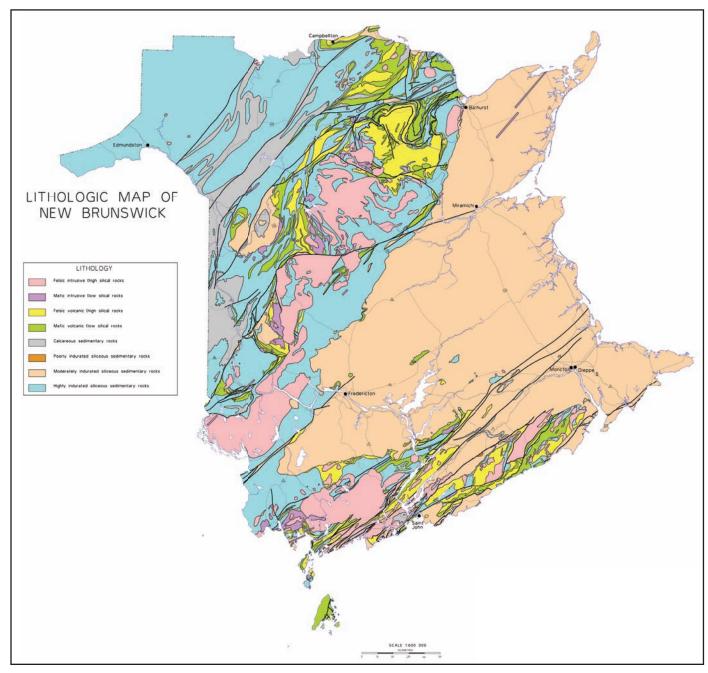


Appendix M: Arsenic Content of Ground Water in New Brunswick, 1994-2008



Source: Department of Environment New Brunswick Groundwater Chemistry Atlas 2009

Appendix N: Lithographic Map of New Brunswick



Source: NB Department of Natural Resources

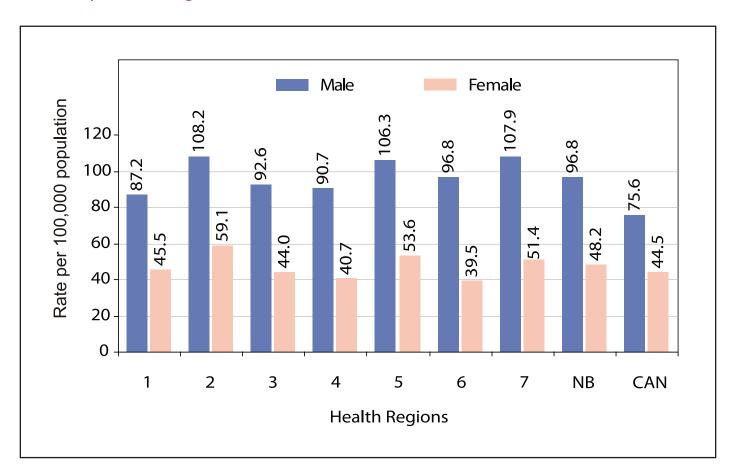
Appendix 0: Comparison of Biomonitoring Results in Unexposed Populations and the Blackville Village Community Sampling November 2008 to February 2009 (n=63)

	Unexposed Populations			Blackville Samples	
		Mean (Range)	n	Range	n
Total Arsenic – Blood (nmol/L)		12.7 (<ld-195)< th=""><th>472</th><th>1.3-395</th><th>63</th></ld-195)<>	472	1.3-395	63
Total Arsenic – Urine (umol/L)	Adults	0.24 (<ld-25.8)<sup>1 0.11 (0.022-0.88)² (10-95th percentile)</ld-25.8)<sup>	318 1542	0.023-4.68	63
	Children	0.094 (0.032-0.62) ³ (10-95 th percentile)	290	0.03-0.20	<5
Inorganic Arsenic – Urine (umol/L)		0.078 (0.26) 50 th (95 th percentile)	1548	0.006-0.070	63
	Children	0.080 (0.20) 50 th (95 th percentile)	292	0.02-0.05	<5

¹ LeBlanc et al. 2004, Quebec City adults (>17 y o).

²Caldwell et al. 2008, US adults (>20 y o). ³ Caldwell et al. 2008, US children (6 -11 y o).

Appendix P: Age Standardized Incidence Rates per 100,000 Population for Lung Cancer by Health Region and Gender, New Brunswick, 1999-2003



Source: NB Health Status Report

Appendix Q: Persons and Organizations Contacted as Part of the Environmental Investigation

Organization	Name and Title		
Department of Fisheries and Oceans	Wayne L. Fairchild, Research Scientist		
NB Department of Natural Resources	Charles Hare, Fisheries Biologist Rodney Mackerin Susan Johnson Geologist		
Canadian Food Inspection Agency	Andrew Jackson Stacy Jewett, Acting Regional Coordinator		
Miramichi Salmon Association	Mark Hambrook, Biologist, President		
Miramichi River Environmental Committee	Harry Collins, Executive Director Omer Mackenzie		
NB Department of Environment	Marc Andre Plourde, Regional Water Planning Officer Mark Boldon, Manager Annie Daigle, Water Resources Specialist Todd Arsenault, Provincial Drinking Water Specialist Don Grass, Manager Nelda Craig, Manager		
Research and Productivity Council (RPC)	Marlene Gregory Peter Crowhurst Ross Kean, Inorganic Analysis		
Blackville residents	Glen Hollowood, Mayor Vye Beckwith Roy McCrae Roland Walls, previous Mayor		
NB Farming Salmon Association	Jamie Smith, Environmental Consultant		
Miramichi Regional Hospital	Blaine Lynch, Director Facilities Management and Information		
Environment Canada	Hélène Dupuis, Environmental Science Advisor		
Health Canada Healthy Environments and Consumer Safety Branch	Shelley Curlew, National Coordination Division Louise White, Regional Health Risk Assessment and Toxicology Specialist James Hardy, Project Officer for the Chemistry and Flammability Division of the Product Safety Programme		