Introduction:

Welcome to the Christmas 2010 edition of Disease Watch NB.

The bulletin has a mixed focus this month, with a lead item on heavy metal testing in clinical practice, an issue that is challenging in most settings but is of increasing concern for many patients.

There are updates about the emerging risk of the old disease, pertussis, for our very young children, an update on cruise ships and norovirus, a reminder of the new Adverse Event Following Immunization (AEFI) reporting system, and a suggestion for the recycling of your Christmas trees this year.

At the end of the first year of production of Disease Watch NB, we thank all our partners for their help in our programs this year, ask them to remind any of their patients yet to have a flu shot to do so, and wish them all a restful festive season. Be safe on the roads this winter. (paul.vanbuynder@gnb.ca).

Heavy metals testing in clinical practice

Case report: A long-standing patient presents to your clinic for a routine follow-up. During this visit, he shares with you his concern that his cottage neighbour's well has recently been found to contain high levels of arsenic. He is worried that he, too, may have been exposed to high levels of arsenic, since he spent the summer months at the cottage and also relies on well water when there. He does not report any signs or symptoms of toxicity. He has not been to the cottage in more than two months.

Given his concern, you decide to request a blood test to measure his exposure to arsenic. The result from his test indicates that his blood arsenic is many times the reference value. You are concerned with this result and contemplate chelation therapy. You also instruct your patient to consider investing in water treatment equipment for the cottage well that is effective in removing arsenic.....

Concerns related to heavy metal exposure can be a daunting challenge for physicians. Such concerns often stem from patients themselves through perceived environmental or occupational concerns. Patients may pressure physicians to request testing leading to difficulties in interpretation and pressure to act on an “elevated” result. It is important to request heavy metal testing only when it is appropriate and to consider carefully which specific metal(s) to test. There are a number of questions that should be considered before requesting testing as well as afterward, in the interpretation of the results.

When should metals testing be considered?

Metals testing can be considered when there is or or is a potential for significant environmental or occupational exposure in the absence of symptoms or clinical signs. It is important to understand the context and details of such an exposure as much as possible (that is, timing and duration, seasonality, route of exposure such as inhalation versus dermal versus ingestion, current versus past exposure, etc.) to determine the likelihood and extent of the problem. Environmental investigation and testing may be appropriate or may already be occurring and can possibly help clarify the relevance of the exposure. In some cases, discussion with the patient and reassurance may be the most appropriate route of action.

Metals testing can also be considered in the presence of signs or symptoms that are compatible with metal toxicity in the context of a wider differential diagnosis. In this setting, a detailed exposure history is essential to determine possible exposure pathways. Health problems related to environmental exposures frequently present as common medical problems (headache, rashes, asthma, difficulty concentrating, fatigue, etc.). It is thus important to understand the clinical presentation of heavy metals toxicity, both for acute and chronic exposures (table 1).

Certain metals, such as essential elements (for example, zinc, copper, manganese, aluminum, iron), are required in minute amounts for normal physiological function. Bio-monitoring results for these metals are difficult to interpret on an individual level, and testing for these should be avoided unless overt toxicity is suspected.

There are numerous resources (see below) available to help you assess the signs and symptoms of potential toxicity, assessing environmental or occupational exposures and interpreting metal bio-monitoring results.
Questions to consider BEFORE requesting metals testing:

When considering testing for a specific metal, the following should be considered:

1 - Is this the right test?

Are there specific forms of the metal to be tested about which we should be concerned, given the type of exposure? Are there specific forms that are more toxic than others, or non-toxic? For example, when considering exposure to chromium, it is the hexavalent form that is of interest as it is the more toxic form.

Case pitfall: Inorganic arsenic is the toxic form that is of concern; organic arsenic stems mainly from dietary exposure (especially seafood) and is of very low toxicity and concern. A request for inorganic analysis is more relevant than organic or total arsenic. Elevated total arsenic may provide misleading information.

2 - Is this the right medium?

What should be tested - Whole blood versus plasma versus serum? What about urine? Hair or nail?

It important to ensure the correct medium is requested and to understand the differences among media. The type of medium chosen can depend on the form of the metal that is of interest or the nature of the exposure (acute versus chronic). For example, cadmium can be measured in both blood and urine. In the context of an acute exposure, elevated blood cadmium levels are useful; however, with chronic exposures urinary cadmium will be more relevant because it reflects integrated exposure over time and total body burden.

Hair and nails are rarely good media to test given their susceptibility to extrinsic contamination; this may confuse the interpretation of any elevated result obtained.

Case pitfall: With regard to arsenic testing, urine testing (spot or, ideally, 24-hour urine) is a more useful measure of exposure than blood.

3 - Is this the right time to test?

Metals have different half-lives in various biological mediums. As an example, mercury has a 60-day half-life in urine yet only about three days in whole blood.

Case pitfall: The half life of arsenic in blood is very short, but urine levels can remain high for weeks after an acute exposure. In this case, many months have passed since the exposure last occurred; therefore, arsenic bio-monitoring will not be useful.

4 - Are special preparations required?

Prior to testing, the reference laboratory should be contacted to clarify the need for any type of special preparation that may be required before specimen collection occurs. For arsenic, it is recommended that patients refrain from consuming seafood for at least five days before specimen collection to avoid falsely elevated results stemming from the low toxicity organic form of arsenic.

Case pitfall: No specific diet was implemented prior to specimen collection; elevated total arsenic in this context does not provide useful information about exposure to relevant toxic forms of arsenic.

Questions to consider AFTER results have been received:

If a decision is made to proceed with testing, an interpretation of the results will be required. If an elevated value is reported, what is the relevance of this result? Is this a health concern for my patient?

1 - Could this be a false positive?

A result above the laboratory’s reference value may be a laboratory error or sample contamination during collection. Revisit the exposure history - are there significant, identified exposures in the patient’s environment that could explain the elevated value? If not, it is appropriate to check with the laboratory and the patient and to confirm this value by retesting.

2 - What is the relevance of this elevated value in health-related terms?

Once an elevated result is received, it is important to understand how the laboratory determines its reference values to assess any potential adverse health impacts. Is it population-based or a small convenience sample? The Canadian Reference Laboratory has two testing paths – medical and environmental/occupational, and unless specified, the former is used. Reference values for this stream are usually determined from a relatively small, non-exposed convenience sample of patients (often local to the lab). This is in contrast with most normal ranges with which we deal in medical tests; from which are derived large samples of people; and which are consistent among laboratories. Reference values based on small convenience samples can vary from one area of the country to another depending on local exposures and higher values may not represent a health concern.

The environmental/occupational stream provides reference values related to occupational standards on acceptable exposure ranges. An occupational reference may be based on risk levels that are higher than those usually accepted on a population level, and this will likely be applicable to healthy adults only and not the more vulnerable groups such as children or the elderly. Reference values used in this type of testing are the same across the country.

Case pitfall: Given the highly elevated value and plausible exposure source, the physician was confident in the result received and obviously concerned with regard to any potential health effects. However, without specifying one or the other, testing would have been conducted through the medical stream; references values to indicate a high value are not necessarily indicative of a health concern.

Case conclusion: After receiving the blood arsenic results, your patient decides to test his water before investing thousands of dollars on a water treatment device. The result from his wells indicates that the arsenic concentration is within Canadian drinking water quality guidelines. Upon further review (and discussion with experts), you realize that the bio-monitoring results are difficult to interpret and request a 24-hour urine specimen for inorganic arsenic (after proper dietary preparation). The results are reported as being within the reference range. Both you and the patient are reassured.
Table 1 Clinical presentation and appropriate testing for common metals

<table>
<thead>
<tr>
<th>Substance</th>
<th>Acute toxicity</th>
<th>Chronic exposure</th>
<th>Testing medium</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arsenic</td>
<td>Nausea, vomiting, diarrhea, Peripheral neuropathy</td>
<td>Hyperkeratosis, hyperpigmentation, Peripheral neuropathy, Anemia, Cancer (skin, lung, liver)</td>
<td>Elevated in smokers, some herbal medicines; Avoid consumption of seafood three to five days before testing</td>
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<tr>
<td></td>
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<td></td>
<td>Urine (24 hour) - request speciation into organic and inorganic forms</td>
</tr>
<tr>
<td>Cadmium</td>
<td>Chemical pneumonitis, Renal failure</td>
<td>Proteinuria, Anemia, Osteomalacia, Emphysema, Lung cancer</td>
<td>High in smokers; Whole blood - for determining recent exposure</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Urine - indicates total body burden</td>
</tr>
<tr>
<td>Chromium</td>
<td>Respiratory and mucus membrane irritation</td>
<td>Sinusitis, nasal septum perforation, Allergic and irritant dermatitis, Asthma, Lung cancer</td>
<td>Prone to sample contamination; Higher in smokers; taking vitamins and minerals; consumption of venison</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Blood - request plasma and RBC, chromium - high RBC indicates chromium VI exposure</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Urine - use in occupational monitoring</td>
</tr>
<tr>
<td>Lead</td>
<td>Abdominal colic, Acute renal failure, Headache, Encephalopathy</td>
<td>Fatigue, Arthralgias and myalgias, Anemia, Hypertension, Peripheral neuropathy, Chronic renal failure, Chronic encephalopathy</td>
<td>Prone to sample contamination (tube and needles)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Whole blood</td>
</tr>
<tr>
<td>Mercury</td>
<td>Chemical pneumonitis, Renal failure</td>
<td>Progressive neurotoxicity, Behavioural changes, Tremor</td>
<td>- No definitive correlation between biologic levels and toxicity</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Urine – for inorganic and elemental mercury toxicity</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Whole blood – test for organic mercury and mercury vapour toxicity; may differentiate organic vs inorganic toxicity</td>
</tr>
</tbody>
</table>

* Harmful or toxic form

Useful resources:
- Agency for Toxic Substances and Disease Registry (ATSDR) at [www.atstdr.cdc.gov](http://www.atstdr.cdc.gov)
- [Unité de Toxicologie Industrielle et Médecine du Travail](http://www.atsdr.cdc.gov)
- Marshall et al; Identifying and managing adverse environmental health effects: 1. Taking an exposure history; Canadian Medical Association Journal; April 16, 2002; 166 (8); p 1049-1055. This is the first article in a series of six articles on environmental health.
- Medical Officers of Health – they can be reached by contacting your local Public Health office.
- WorksafeNB medical staff. Contact Dr. Douglas Margison, chief medical officer, 506-738-4053

The impending pertussis outbreak in New Brunswick

Pertussis (whooping cough) is a highly infectious respiratory disease associated with chronic cough and pneumonia. The disease is named for the characteristic sound produced when affected individuals attempt to inhale; the whoop originates from the inflammation and swelling of the laryngeal structures that vibrate when there is a rapid inflow of air during inspiration.

The first outbreaks of whooping cough were described in the 16th century. The bacterium responsible for the infection, *Bordetella pertussis*, was not identified until 1906. In the pre-vaccination era (during the 1920s and 1930s), there were more than 250,000 cases of whooping cough, with up to 9,000 deaths, in the United States each year. In the 1940s, a whole cell pertussis vaccine, combined with diphtheria and tetanus (DPT) was introduced. By 1976, the incidence of whooping cough in the United States had decreased by more than 99 per cent. In Canada through immunization, and during the last 50 years, its incidence has decreased by more than 90 per cent. This vaccine was not used in adults due to its high reactogenicity, but we now have available acellular forms of the vaccine suitable for adolescents and adults (Tdap).

During the 1980s, the incidence of whooping cough began to increase and has risen steadily, with outbreaks typically occurring every three to five years in the United States. In the outbreak that occurred in 2005, 25,616 cases were reported according to the United States Centers for Disease Control and Prevention (CDC). In 2008, more than 13,000 cases of whooping cough were reported in the United States, resulting in 18 deaths. In 2010, a pertussis epidemic was declared in California. The California Department of Public Health warned in June 2010 that the state was on pace to suffer the most illnesses and deaths due to whooping cough in the past 50 years. In the previous outbreak of 2005, California recorded 3,182 cases and eight deaths, but this year, it has already had more than 6,000 cases and 10 deaths, all in children younger than three months. An outbreak in Saskatchewan this year has claimed the lives of five children younger than three months.

Unimmunized or incompletely immunized young infants are particularly vulnerable to the infection and its complications, which can include pneumonia and seizures. For maximum protection against pertussis, children need five DTaP shots. The first three vaccinations are given at two, four and six months. The fourth is given at 18 months, and a fifth is given when a child enters preschool, at four years. Adolescents in Grade 9 are given a school based Tdap booster, and adults who did not receive Tdap as an adolescent should get one dose of Tdap. The easiest way for adults to ensure immunity is to get the Tdap vaccine instead of their next regular tetanus booster. (TheTd shot is recommended every 10 years).

To protect their infants, most pregnant women who were not previously vaccinated with Tdap should receive one dose of Tdap postpartum before leaving the hospital or birthing centre. Being vaccinated with Tdap is especially important for mothers and families with new infants as well as all people caring for newborns.
The New Brunswick situation:

The epidemiology of pertussis in New Brunswick mimics that in the United States with outbreaks in 1995, 1998-99, and 2004 (Figure 1). In non-outbreak years, the number of cases in children younger than one (the highest risk group for hospitalizations and death) is as low as two per year. In the three most recent outbreak years the number of cases in children younger than one varied between 16 and 45 cases (figure 2).

New Brunswick is overdue for a pertussis outbreak. It is highly probable that, in the next year or two, a cluster of 30 or so children younger than one year will contract pertussis; many will be hospitalized and some will die. The only way to protect these infants is a “cocoon strategy” to decrease the likelihood of exposure. Data from Australian and North American studies show that more than 40 per cent of these children contract the disease from their mother and another 25 per cent from another family member.

Only six per cent of New Brunswick babies are born to mothers younger than 20 who may potentially be immune after receiving an adolescent dose of vaccine. The other 94 per cent are too old to have received the adolescent school booster since its introduction and their children and newborns are at risk.

Commencing January 1, 2011 New Brunswick will endeavour to protect young infants during the upcoming epidemic by offering free Tdap boosters to all mothers post-partum and to their partners before birth. It is hoped that all practitioners seeing pregnant women will advise them of this need and take steps to see their partners to immunize them as soon as possible.

Consideration is being given to expanding this access to free Tdap to other close caregivers and replacing all adult Td boosters with doses of Tdap. This further expansion will be dependent on availability of vaccine doses and funds. In the interim, although ineligible to receive publicly funded vaccine, all persons other than parents, with close contact with very young children, are advised to seek a booster dose.

Noroviruses and cruise ships

In October 2010, a cruise ship with more than 2,000 passengers, arrived in the Port of Saint John1, carrying about 40 passengers and crew suffering from gastrointestinal illness (GI). Although this particular event was not considered to be an outbreak (defined by Health Canada as an attack rate of at least two per cent of passengers or two per cent of the crew2), outbreaks of GI on cruise ships are relatively common. Cruise ships carry thousands of passengers and crew in shared spaces for extended periods and, for this reason, can facilitate rapid spread of communicable diseases such as GI. Noroviruses (commonly called Norwalk viruses) are particularly contagious and are transmitted easily from person-to-person in confined environments. The attack rate of noroviruses in such enclosed spaces can be very high without strict infection control measures as the infectious dose of this virus is fewer than 100 particles, and it is resistant to many common control mechanisms.

Noroviruses are a group of viruses that cause sudden onset of diarrhea, nausea, vomiting and/or stomach cramps in humans. Fever, chills, headache, muscle aches and fatigue may also occur. People are infectious from the time of symptom onset and for up to two weeks following recovery. Symptoms typically develop 12 to 48 hours after exposure and last for eight to 12 hours. Full recovery usually occurs within 48 hours3.

Noroviruses are found in the stool and vomit of infected people. The virus may be transmitted through contaminated food or water, contact with an infected person, or by touching a contaminated surface. Noroviruses are resilient and can survive on hard surfaces, such as door handles, for up to 12 hours and on carpet for up to 12 days4.

This resilience, and continued shedding by staff who do not leave the ship between cruises, has been the cause of some cruise ships...
Health Canada operates a voluntary Cruise Ship Inspection Programme (CSIP) to prevent and control outbreaks, such as those caused by noroviruses, on cruise ships. All vessels that visit Canadian ports undergo unannounced, annual inspections of their water quality, food safety, environmental sanitation, and incidence rates of GI. Cruise ships receive a score, where a “passing” score is 86 out of a possible 100 points. Results of these inspections are publicly available on Health Canada’s website, www.hc-sc.gc.ca/hl-vs/travel-voyage/general/ship-navire-eng.php.

When travelling on cruise ships, good personal hygiene practices are vital in the prevention of GIIs such as those caused by noroviruses. Frequent hand washing is the single most important method of preventing infection, especially after using the bathroom or changing diapers and before handling food.

If illness occurs, infected individuals should notify an on-board health-care professional, stay in their rooms and avoid contact with others until they are well again. Dehydration caused by illness can be prevented by drinking plenty of fluids and taking oral rehydration salts. Young children, the elderly, and people with compromised immune systems are particularly susceptible to dehydration.

For more information about noroviruses, visit the Public Health Agency of Canada website, www.phac-aspc.gc.ca/id-mi/norovirus-eng.php.

References:

Syphilis Outbreak in New Brunswick

The province of New Brunswick (NB) is experiencing an outbreak of infectious syphilis. Historically, NB has reported less than five cases of infectious syphilis per year; however, this number has steadily increased since 2008. To date, 33 cases have been reported in 2010, representing a nine-fold increase in the incidence rate of syphilis since 2007 (0.5 vs 4.4 per 100 000).

Of the cases reported in 2010, 17 (52%) were primary or secondary syphilis, 5 (15%) were early latent syphilis, and 11 (33%) are unspecified at this point. Thirty (91%) of 33 cases are male and three cases (9%) are female, including two pregnant women. The mean age of all cases is 33.3 years with a range of 18-49 years. The majority of cases appear to be among those aged 20-24 and 35-44 years. At least half of the male cases reported MSM activities.

A provincial Outbreak Control Team has been formed and enhanced surveillance and control measures are currently being implemented.

The CDC urges clinicians to increase your diagnostic alert for syphilis during this outbreak. If you see a patient with suspected syphilis, please consult infectious diseases specialists (if available) and send appropriate sample(s) to your laboratory for testing. Also please make sure that a referral is made to the local Public Health unit so that investigation questionnaire is completed and that contact tracing is carried out. Practitioners are reminded that all pregnant women should be tested for syphilis at the first antenatal visit.

Fighting the pandemic with Christmas trees

The provincial government successfully minimized the impact of the pandemic last year with a combination of vaccine and the use of the anti-viral neurominidase inhibitor oseltamivir, (Tamiflu) thought to be effective in ameliorating disease if given sufficiently early.

The main ingredient of oseltamivir, a compound called shikimic acid, is usually obtained from star anise, an unusual star-shaped fruit that grows on small trees native to China. Prices of the fruit skyrocketed when anxiety over a possible human outbreak of avian flu (H5N1) first escalated in recent years.

Shikimic acid also comes from pine trees in Maine. Researchers at the University of Maine at Orono have found a new and relatively easy way to extract the key ingredient in the drug Tamiflu from pine tree needles. Shikimic acid can be removed from the needles of white pine, red pine and other conifer trees simply by boiling the needles in water. Additional testing is needed, and it remains to be seen if the process can be applied commercially in the private sector.

The needles of spruce and fir trees also contain a fairly high concentration of shikimic acid. A small Canadian pharmaceutical
company is collecting the needles from discarded Christmas trees to process them and convert them to the oseltamivir precursor. These trees, previously converted into mulch and potting soil, are instead forming the basis of an additional future pandemic response.

**Antibody-rich bovine colostrums reduces flu morbidity and deaths**

Antibody-rich bovine colostrums could be a simple and cheap solution for preventing and treating influenza pandemics, Australian researchers say. Early trials of intranasal bovine colostrums derived from cows that have been vaccinated to produce high levels of IgGs show that the colostrum has a significant effect in reducing influenza morbidity and mortality when used just once a week.

The NHMRC sponsored research carried out at Melbourne University suggests that hyperimmune bovine colostrums could be a useful adjunct to influenza vaccination for boosting immunity levels, as well as a more practical alternative to antiviral drugs.

In preliminary studies they showed that a single intranasal dose of hyperimmune colostrums reduced the severity and duration of established influenza infection in mice. It was also effective as prophylaxis, allowing pre-treated mice to survive an otherwise lethal dose of influenza virus. The author says production of hyperimmune colostrums could easily be scaled up using current dairy production methods and animal husbandry techniques. One cow vaccinated with the latest influenza strains could produce enough colostrum within weeks to treat 500 people.

“Due to the relative low cost and high volume capability or production, this new approach represents a significant tool for individual and large scale public health management of influenza in humans”, they concluded.

**Farewell Carol Sharpe and Mark Wies**

With regret, the editorial team of Disease Watch NB says farewell, to the two senior marketing personnel integral to the development of this bulletin.

Carol and Mark were part of the management team that led the professional communication responses to the pandemic response last year, led the Communications New Brunswick team that revitalised public health web activity, introduced positive marketing processes to public health programs and oversaw the production of the ongoing Disease Watch bulletins.

Their commitment to enhancing public health messaging and getting our message out to our colleagues will be greatly missed. We wish them both well in their future endeavours.

**AEFI INFORMATION**

All health-care professionals in New Brunswick who administer vaccines and/or care for patients who may have had an Adverse Event Following Immunization (AEFI) are required by law to report the event to a medical officer of health within one week of event identification.

An AEFI is any unwanted medical event that follows immunization. Any adverse symptoms or signs of disease following immunization are classified as an AEFI.

All immunizers (Public Health and non-Public Health), upon becoming aware of a potential AEFI, should gather all necessary information, document the event on the NB AEFI report form and forward it to their local Public Health office. However, the AEFI data can also be telephoned in.

The NB AEFI reporting form with corresponding user guide can be obtained from either the GNB website: www.gnb.ca/health or your local Public Health office.

Please remember: that timeliness of AEFI reporting is very important because it facilitates effective risk management and allows to address any safety concerns quickly and efficiently.