Vibrio cholerae causes profuse, watery diarrhea, which may be life-threatening. The licensed parenteral vaccine has limited effectiveness and is not recommended for Canadians travelling to endemic areas. An oral cholera vaccine, CVD 103-HgR (Swiss Serum and Vaccine Institute), is available in Canada through the Emergency Drug Release Program of Health Canada. This brief evidence-based medicine statement addresses the use of the unlicensed product. A full statement will be issued following licensure of the oral vaccine. The World Health Organization does not currently have a specific recommendation for the use of this vaccine in the travelling public. At the moment, no country requires proof of cholera vaccination as a condition for entry. In addition, the International Certificate of Vaccination no longer provides a specific space for recording of cholera vaccination.

The Oral Cholera Vaccine

a. Safety randomized, controlled studies have now been carried out in at least 4,000 subjects in a number of cholera-endemic and non-endemic areas and have demonstrated good tolerance and safety of the product. The side effect profile was similar to the control (placebo) groups except for mild diarrhea, which occurred in 6.4% of those vaccinated.

b. Immunogenicity — Several studies have shown a good immune response, with seroconversion rates over 90% following a single oral dose of the vaccine. Seroconversion occurred as early as 8 days after administration of the vaccine and lasted 6 months. Protective efficacy has been tested in volunteers in challenge studies, demonstrating protection against the classic biotype in 82% to 100% of subjects, and in 62% to 67% in participants exposed to the El Tor biotype.

There is no cholera vaccine currently available that has been shown to be protective against the O139 Bengal strain, which has recently emerged in South Asia and has spread to South East Asia.

Cholera Disease Risk Assessment

The utility of a vaccine depends not only upon its protective efficacy and safety profile, but also upon the risk of infection and disease outcomes (morbidity and mortality), and the cost of the vaccine. The estimated risk of cholera disease in European or North American travellers to endemic areas is 1 to 2 cases per million trips. As has been shown in a recent cholera vaccination decision analysis, for the vaccine to be cost-effective in the prevention of cholera, the risk of disease would have to be very much higher than has been recognized recently. Currently, there is no recommendation for the routine use of the licensed, parenteral vaccine for the prevention of cholera in Canadians travelling to endemic areas. A detailed, individual risk assessment would be required to detect an individual at higher risk for cholera acquisition related to travel prior to consideration for cholera vaccination with any product.
Oral Cholera Vaccination in the Prevention of Traveller’s Diarrhea

During vaccine efficacy trials for the whole-cell cholera vaccine, a reduction in the occurrence of enterotoxigenic Escherichia coli (ETEC)-associated diarrhea was noted as a secondary outcome in the vaccinated population. It is important to note the following:

1. This is a different vaccine product than the oral cholera vaccine that is under consideration for licensure.
2. There have been no studies, published to date, using any oral cholera vaccine for the prevention of ETEC-associated diarrhea in travellers.

Recommendations

1. The use of oral cholera vaccine for the prevention of cholera in travellers to endemic areas can not be supported at this time [strength of recommendation: Category C; quality of evidence: grade II (see also Appendix I)].
2. There is insufficient data to support use of the oral cholera vaccine in the prevention of traveller’s diarrhea due to ETEC [strength of recommendation: Category C; quality of evidence: grade II (see also Appendix I)].
3. Travellers are advised to follow the recommendations of CATMAT for the prevention and treatment of traveller’s diarrhoea [strength of recommendation: Category B; quality of evidence: grade I (see also Appendix I)].

Using unlicensed vaccines: Physicians are reminded that it is advisable to obtain written, informed consent prior to administering an unlicensed product and that it is a condition of the Emergency Release Program to inquire about and report any significant adverse effects of vaccination.

References


Appendix 1

Categories for strength of each recommendation

<table>
<thead>
<tr>
<th>CATEGORY</th>
<th>DEFINITION</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Good evidence to support a recommendation for use.</td>
</tr>
<tr>
<td>B</td>
<td>Moderate evidence to support a recommendation for use.</td>
</tr>
<tr>
<td>C</td>
<td>Poor evidence to support a recommendation for or against use.</td>
</tr>
<tr>
<td>D</td>
<td>Moderate evidence to support a recommendation against use.</td>
</tr>
<tr>
<td>E</td>
<td>Good evidence to support a recommendation against use.</td>
</tr>
</tbody>
</table>

Categories for quality of evidence on which recommendations are made

<table>
<thead>
<tr>
<th>GRADE</th>
<th>DEFINITION</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Evidence from at least one properly randomized, controlled trial.</td>
</tr>
<tr>
<td>II</td>
<td>Evidence from at least one well-designed clinical trial without randomization, from cohort or case-controlled analytic studies, preferably from more than one centre, from multiple time series, or from dramatic results in uncontrolled experiments.</td>
</tr>
<tr>
<td>III</td>
<td>Evidence from opinions of respected authorities on the basis of clinical experience, descriptive studies, or reports of expert committees.</td>
</tr>
</tbody>
</table>

CHOLERA IN BRITISH COLUMBIA

We report on three laboratory-confirmed cases of cholera due to toxigenic *Vibrio cholerae* O1 El Tor Ogawa that occurred in British Columbia during the first 2 months of 1995. The isolated organisms were all sensitive to tetracycline, trimethoprim/sulfamethoxazole, and ciprofloxacin.

**Case 1**

This 38-year-old male had travelled alone to San Salvador in El Salvador to visit family. He became ill with vomiting and diarrhea en route home to British Columbia on 13 January, 1995. He was admitted to hospital with classical rice-water stools within a few hours of his arrival home. He was rehydrated with intravenous fluids and received ciprofloxacin during his 3-day hospitalization. He was aware that there had been cholera cases in the poorer districts of San Salvador and had been careful to avoid high-risk foods, such as seafood and street vendor items. He drank mainly bottled water. He had brought back dried fruits from San Salvador, which his wife had partially consumed without any ill effects. No other household members in San Salvador or in B.C. were reportedly symptomatic with diarrheal illness.

**Case 2**

This 30-year-old male had travelled with his wife to San Salvador in El Salvador to visit family. They were not related to Case 1. He developed diarrhea en route home to B.C. on 5 January, 1995, after consuming orange juice and *pupusas* (stuffed tortillas) the day before. He was employed as a cook and returned to work despite symptoms. A stool culture was ordered on 10 January by his family doctor because of persistent diarrhea. He was managed as an outpatient and treated with oral trimethoprim/sulfamethoxazole. He had brought back with him some cheese that family members had consumed. No household members in San Salvador or in B.C. were reportedly symptomatic.

**Case 3**

This 78-year-old female had travelled to Bali in Indonesia for a vacation with her husband. She became ill with vomiting and copious watery diarrhea on 7 February, 1995, after eating a seafood meal at their hotel in Bali the previous day. She remained ill during her return journey home to B.C. and was directly admitted to hospital on 11 February on arrival. She was treated for dehydration and was discharged after 2 days. She did not receive any antibiotics; follow-up stool cultures were negative. Her husband had not been symptomatic and stool cultures were negative for *V. cholerae*. A package of cookies had been brought back from Indonesia.

**Discussion**

Cholera is an internationally notifiable and quarantinable disease subject to the International Health Regulations. The Laboratory Centre for Disease Control (LCDC) made obligatory case reports to the World Health Organization (WHO) for these cases. LCDC also notified public health authorities in the United States as a courtesy because all cases had been symptomatic during stopovers in this country. El Salvador and Indonesia are listed as cholera-infected countries by the WHO. However, the province of Bali was not considered an infected area within Indonesia.(1)

**References**

consumption of raw sea food, could be identified in one case, the method of acquisition for the other cases is undefined.

As described in the attached article, cholera remains one of the three, internationally reportable communicable diseases under the *International Health Regulations*, the other two being plague and yellow fever. Following reports to the WHO of cholera acquired in Bali, the organization sent a consultant to the area to review the situation with local government officials. No localized disease focus was identified and Bali remains officially a non-infected area.

Cholera remains a serious concern in terms of both its medical impact as well as the commercial implications related to the marketing of food items and the impact on tourism. Easily carried across international borders by modern modes of transportation, the O139 Bengal serogroup first observed in Asia in 1992, was isolated within a matter of months from Europe and North America. The rapid global transport of this disease has become a paradigm for describing the potential implications of newly emerging infectious diseases.

Risk reduction by behavioral modification, such as avoiding the consumption of unpurified water, raw sea food, raw or uncooked items, and other educational measures remain the standard approaches for dealing with travellers destined to endemic areas. Routine immunization of most travellers is not indicated and proof of vaccination against the disease is not required for international travellers. Those who will have ongoing close contact with the local population in areas of high incidence of cholera, for example health care workers or workers in refugee camps, may benefit from immunization.

**References**

3. PAHO. *Cholera situation in the Americas.* Update No 14, 1996, Washington, DC.
International Notes

CHOLERA IN AFRICA

Several Western African countries have reported cholera cases to the World Health Organization (WHO) during the first 2 months of 1996 and, although some have recorded rather higher figures than at other times, control measures are in place. The media have reported these outbreaks in various ways, but their reports have given rise to a certain amount of fear amongst travellers to these countries.

WHO would like once again to remind travellers that cholera outbreaks should not prevent them from visiting a country provided that the usual precautions regarding food and drinking water are taken. These are as follows:

- Drink only water that has been boiled or disinfected with chlorine or iodine. Products for disinfecting water are generally available in pharmacies. Beverages such as hot tea or coffee, wine, beer, carbonated water or soft drinks, and bottled or packaged fruit juices are also usually safe to drink.
- Avoid ice, unless you are sure that it is made from safe water.

NEW VARIANT OF CREUTZFELDT-JAKOB DISEASE (V-CJD)—FRANCE

The second edition of these guidelines has been updated to reflect currently recognized containment requirements and operational practices and is consistent with such practices worldwide. Current legislation relevant to microbiologic laboratories is also included.

The objective of these guidelines is to provide a technical document for those who design, build, operate or work in laboratories in which human pathogens are grown for research or development purposes. The focus, therefore, is on the use of bacteria, viruses, parasites, fungi and other infectious agents, which are pathogenic to humans, and their appropriate handling according to their risk category.

Copies of the second edition are available by faxing a request to the Office of Biosafety, Laboratory Centre for Disease Control, (613) 941-0596.

Announcement

LABORATORY BIOSAFETY GUIDELINES

The objective of these guidelines is to provide a technical document for those who design, build, operate or work in laboratories in which human pathogens are grown for research or development purposes. The focus, therefore, is on the use of bacteria, viruses, parasites, fungi and other infectious agents, which are pathogenic to humans, and their appropriate handling according to their risk category.

Copies of the second edition are available by faxing a request to the Office of Biosafety, Laboratory Centre for Disease Control, (613) 941-0596.