



ISBN 1188-4169

# Canada Communicable Disease Report



Vol . 22-10

Date of publication: 15 May 1996

Contained in this FAX issue: (No. of pages: 6)

Official page numbers:

CATMAT AND NACI—PRELIMINARY CONJOINT STATEMENT ON ORAL CHOLERA VACCINATION . . . . .	F-1	73-75
CHOLERA IN BRITISH COLUMBIA . . . . .	F-3	75-78
CHOLERA IN AFRICA . . . . .	F-5	79
NEW VARIANT OF CREUTZFELDT-JAKOB DISEASE (V-CJD)—FRANCE . . . . .	F-5	79-80
ANNOUNCEMENT . . . . .	F-5	80

For reference purposes, citing should refer to the page numbers of the printed copy and not to those of the FAX copy (F-#).

## The Committee to Advise on Tropical Medicine and Travel (CATMAT) and the National Advisory Committee on Immunization (NACI)

### PRELIMINARY CONJOINT STATEMENT ON ORAL CHOLERA VACCINATION

*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<sup>(1)</sup> (see also Appendix I) 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

- 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<sup>(2,3,4,5,6)</sup> 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<sup>(2,3,4,5)</sup>.
- Immunogenicity* — Several studies have shown a good immune response, with seroconversion rates over 90% following a single oral dose of the vaccine<sup>(2,3,4,5,6,7,8)</sup>. Seroconversion occurred as early as 8 days after administration of the vaccine and lasted 6 months. Protective efficacy has been tested in volunteers in oral

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<sup>(9)</sup>. As has been shown in a recent cholera vaccination decision analysis<sup>(9)</sup>, 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.



Health Canada Santé Canada

Canada

## 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<sup>(10)</sup>. 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)]<sup>(8)</sup>.
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)]<sup>(9)</sup>.
3. Travellers are advised to follow the recommendations of CATMAT for the prevention and treatment of traveller's diarrhea [strength of recommendation: Category B; quality of evidence: grade I (see also Appendix I)]<sup>(11)</sup>.

**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

1. MacPherson DW. *Evidence-based medicine*. CDR 1994;20:145-47.
2. Cryz SJ, Levine MM, Kaper JB et al. *Randomized, double-blind, placebo-controlled trial to evaluate the safety and immunogenicity of the live cholera vaccine strain CVD 103-HgR in Swiss adults*. Vaccine 1990;8:577-80.
3. Kotloff KL, Wasserman SS, O'Donnell S et al. *Safety and immunogenicity in North Americans of a single dose of live oral cholera vaccine CVD 103-HgR: results of a placebo-controlled, double-blind crossover trial*. Infect Immun 1992;60:4430-32.
4. Levine MM, Herrington D, Losonsky G et al. *Safety, immunogenicity, and efficacy of recombinant live oral vaccines, CVD 103 and CVD 103-HgR*. Lancet 1988;2:467-70.
5. Su-Arehawaratana P, Singharaj P, Taylor DN et al. *Safety and immunogenicity of different immunization regimens of CVD 103-HgR live oral cholera vaccine in soldiers and civilians in Thailand*. J Infect Dis 1992;165:1042-48.

## Appendix 1

Categories for strength of each recommendation	
CATEGORY	DEFINITION
A	Good evidence to support a recommendation for use.
B	Moderate evidence to support a recommendation for use.
C	Poor evidence to support a recommendation for or against use.
D	Moderate evidence to support a recommendation against use.
E	Good evidence to support a recommendation against use.
Categories for quality of evidence on which recommendations are made	
GRADE	DEFINITION
I	Evidence from at least one properly randomized, controlled trial.
II	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.
III	Evidence from opinions of respected authorities on the basis of clinical experience, descriptive studies, or reports of expert committees.

6. Suharyono, Simanjuntak C, Witham N et al. *Safety and immunogenicity of single-dose live oral cholera vaccine CVD 103-HgR in 5 to 9-year-old Indonesian children*. Lancet 1992;340:689-94.
7. Kaper JB, Morris JG, Levine MM. *Cholera*. Clin Microbiol Rev 1995;8:48-86.
8. Tacket CO, Losonsky G, Nataro JP et al. *Onset and duration of protective immunity in challenged volunteers after vaccination with live oral cholera vaccine CVD 103-HgR*. J Infect Dis 1992;166:837-41.
9. MacPherson DW, Tonkin M. *Cholera vaccination: a decision analysis*. Can Med Assoc J 1992;146:1947-52.
10. Peltola H, Siitonen A, Kyronseppa H et al. *Prevention of traveller's diarrhoea by oral  $\beta$ -subunit/whole-cell cholera vaccine*. Lancet 1991;338:1285-89.
11. Committee to Advise on Tropical Medicine and Travel. *Statement on travellers' diarrhea*. CDR 1994;20:149-55.

## 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<sup>(1)</sup>.

Cholera is spread by contaminated food and water; infection usually requires ingestion of a large number of organisms. Of those infected, 80% are asymptomatic and less than 5% have severe disease characterized by voluminous, painless, rice-water stools<sup>(2)</sup>. A 3-day course of tetracycline or doxycycline is the recommended treatment of choice for symptomatic infection; antimicrobial therapy shortens the course of diarrhea and eradicates the vibrios. Replacement of fluids remains the cornerstone treatment for all diarrheal diseases including cholera. Rehydration with intravenous Ringer's lactate or oral rehydration salt solution is recommended for appropriate replacement of both fluid and electrolytes. Treatment is not recommended for asymptomatic cholera-exposed persons in developed countries<sup>(3,4)</sup>.

Enterotoxin-producing *V. cholerae* serogroup O1 and O139 have caused epidemics. *V. cholerae* O1 El Tor has been responsible for the seventh cholera pandemic starting in 1961 in Sulawesi, Indonesia<sup>(2)</sup>. *V. cholerae* O1 El Tor Inaba initially caused the epidemic in the Americas that started in Peru in 1991<sup>(4,5)</sup>. Both Inaba and Ogawa serotypes have subsequently been circulating in the Americas<sup>(6)</sup>. *V. cholerae* O139 has caused widespread illness in Asia since 1993<sup>(7,8)</sup>. Although toxigenic and non-toxigenic strains that are not O1 nor O139 can cause sporadic diarrheal disease, they are not currently associated with epidemics.

In B.C. from 1 January, 1991 to 31 December, 1994, only five cases of cholera were identified. Four were due to *V. cholerae* O1 El Tor Ogawa and were associated with international travel. Travel to Mexico and Peru was specified in two of these cases. One fatal case was due to *V. cholerae* O139 and was associated with travel to India. There are no endemic foci of cholera in Canada; all cholera cases in Canada are imported. In the United States, the estimated rate of cholera was 0.3 per 100,000 air travellers returning from South America in 1991 and 0.2 per 100,000 air travellers returning from cholera-endemic countries in 1982<sup>(9)</sup>. Outbreaks of cholera in the U.S. have been associated with imported foods, including food brought into the country in travellers' luggage<sup>(9)</sup>. These three B.C. cases brought back food from their travels; this reinforces the need for public health personnel to specifically question cholera cases about informal importation of food items and to assess the risk of these items for transmission of cholera.

### Acknowledgements

We would like to thank the staff from the Vancouver Health Department, Capital Regional District Health Department, and Boundary Health Unit, Dr. J. Busser, Langley Memorial Hospital, and Island Medical Laboratories for providing information about the cholera cases in B.C. in 1995. We would also like to thank Dr. B. Gushulak, LCDC, for his assistance.

### References

1. WHO. *List of infected areas*. Wkly Epidemiol Rec 1994;69:370-72.
2. Black RE. *Cholera*. In: Last JM, Wallace RB, eds. *Maxcy-Rosenau>Last public health and preventive medicine*. 13th ed. Norwalk, Conn: Appleton & Lange 1992:176-78.
3. Besser RE, Felkin DR, Eberhart-Phillips JE et al. *Diagnosis and treatment of cholera in the United States*. JAMA 1994;272:1203-05.

4. Gotuzzo E, Cieza J, Estremadoyro L. *Cholera: lessons from the epidemic in Peru*. Infect Dis Clin North Am 1994;8:183-205.
5. CDC. *Update: Cholera - western hemisphere 1992*. MMWR 1993;42:89-91.
6. Vugia DJ, Rodriguez M, Vargas R et al. *Epidemic cholera in Trujillo, Peru, 1992: utility of a clinical case definition and shift in *Vibrio cholerae* O1 serotype*. Am J Trop Med Hyg 1994;50:566-69.
7. CDC. *Imported cholera associated with a newly described toxigenic *Vibrio cholerae* O139 strain - California 1993*. MMWR 1993;42:501-03.
8. CDC. *Addressing emerging infectious disease threats: a prevention strategy for the United States*. MMWR 1994;43(RR-5):1-18.
9. Weber JT, Levine WC, Hopkins DP et al. *Cholera in the United States, 1965-1991: risks at home and abroad*. Arch Intern Med 1994;154:551-56.

**Source:** DH Werker, MD, BC Federal Field Epidemiologist, AS King, Epidemiology Services, BC Centre for Disease Control, MT Kelly and T Matheson, BC Provincial Laboratory, AA Bell, MD, Provincial Epidemiologist, Vancouver, B.C.

## Editorial Comment

The seventh pandemic of *Vibrio cholera* O1, biotype El Tor, began in Indonesia in 1961. By 1991 it had reached Central and South America representing the return of this disease after a century of absence<sup>(1)</sup>. In 1994, approximately 384,403 cases of this disease were reported to the World Health Organization (WHO) from 94 countries<sup>(1)</sup>. A total of 10,692 deaths from cholera were reported in 1994. Cases continued to be reported from areas of the Newly Independent States of the former USSR<sup>(2)</sup>.

The Pan American Health Organization (PAHO) has recently reported that, 6 years into the epidemic in the western hemisphere, cholera continues to spread in Latin America. Since the beginning of the epidemic in Peru in 1991, more than 1.3 million cases and 11,339 deaths have been reported in Central and South America. In 1995, 85,802 cases and 847 deaths were reported from 14 countries in the region. This is a decrease from the previous year when 195,574 cases and 1,321 deaths were reported<sup>(3)</sup>.

During 1995, Quarantine Health Services at the Laboratory Centre for Disease Control was notified, by three provinces, of eight cases of cholera imported into Canada. The cases, four females and four males, ranged from 5 to 78 years of age. Three cases were acquired in El Salvador, three in Bali, Indonesia, and one in Mexico, while the origin of the remaining case remains unknown. Culture reports have revealed *Vibrio cholera* serogroup O1, biotype El Tor. While specific risk factors, i.e., the

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<sup>(4)</sup>.

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<sup>(5)</sup>.

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<sup>(6)</sup>.

## References

1. Kaper JB, Morris JG, Levine MM. *Cholera*. Clin Microbiol Rev 1995;8:48-86.
2. World Health Organization. *Cholera in 1994*. Wkly Epidemiol Rec 1995;70:201-08.
3. PAHO. *Cholera situation in the Americas*. Update No 14, 1996, Washington, DC.
4. World Health Organization. *Criteria used in compiling the infected area list*. Wkly Epidemiol Rec 1995;70:95.
5. Centers for Disease Control and Prevention. *Assessing emerging infectious disease threats: a prevention strategy for the United States*. Atlanta, Georgia: U.S. Department of Health and Human Services, Public Health Service, 1994.
6. National Advisory Committee on Immunization. *Canadian immunization guide*. 4th ed. Ottawa, Ont: Health Canada, 1993. (Supply and Services Canada, Cat. no. H49-8/1993E).

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 among 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.**

- **Eat food that has been thoroughly cooked and is still hot when served.** Cooked food that has been held at room temperature for several hours and served without being reheated can be an important source of infection.
- **Avoid raw seafood and other raw foods,** except fruits and vegetables that you have peeled or shelled yourself. Remember: Cook it, peel it, or leave it.
- **Boil unpasteurized milk before drinking it.**
- **Ice cream from unreliable sources is frequently contaminated and can cause illness. If in doubt, avoid it.**
- **Be sure that meals bought from street vendors are thoroughly cooked in your presence and do not contain any uncooked foods.**

If travelling with family members or others, ensure that they also take these precautions. Infants < 6 months of age who are breast-fed, and receive no other foods or drinks, have a low risk of infection.

Source: WHO Epidemiological Record, Vol 71, No 10, 1996.

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

The reported occurrence in the United Kingdom of a new variant of Creutzfeldt-Jakob disease (V-CJD) has led to the re-examination of cases identified in France in latter years. In 1992-1994, in addition to cases observed in patients formerly treated by growth hormone extracts, 135 cases were identified (about 0.8 cases per million population per year). Of the five cases concerning younger subjects, two were genetically determined and one was subsequent to a human dura mater graft; no iatrogenic or genetic risk factor could be identified in two cases:

- a 37-year-old male, for whom no specific investigation results are available;
- a 26-year-old male, who died recently in Lyons and in whom histopathologic observations are similar to those reported from

the United Kingdom. The case is still under investigation and no new conclusions can be drawn at present.

The protective mechanisms set up in France since 1990 are regularly assessed and relevant WHO recommendations are rigorously applied. CJD has been included among the compulsory notifiable diseases; the creation of an expert committee at the Ministry of Health and the clinical and neuropathologic reassessment of cases observed in recent years will assist in identifying new or hitherto unsuspected elements concerning this rare disease.

Source: WHO Weekly Epidemiological Record, Vol 71, No 16, 1996.

Announcement

LABORATORY BIOSAFETY GUIDELINES

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.**

The Canada Communicable Disease Report (CCDR) presents current information on infectious and other diseases for surveillance purposes and is available through subscription. Many of the articles contain preliminary information and further confirmation may be obtained from the sources quoted. Health Canada does not assume responsibility for accuracy or authenticity. Contributions are welcome (in the official language of your choice) from anyone working in the health field and will not preclude publication elsewhere.

Scientific Advisors	Dr. John Spika	(613) 957-4243
	Dr. Fraser Ashton	(613) 957-1329
Editor-in-Chief	Eleanor Paulson	(613) 957-1788
Assistant Editor	Nicole Beaudoin	(613) 957-0841
Desktop Publishing	Joanne Regnier	

Submissions to the CCDR should be sent to the Editor-in-Chief at the following address:  
Laboratory Centre for Disease Control, Tunney's Pasture, Ottawa, Ontario K1A 0L2.

To subscribe to this publication, please contact:  
Information Technology Group      Tel. No.: (613) 731-9331, ext. 2028  
Canadian Medical Association      FAX:      (613) 731-9102  
P.O. Box 8650  
Ottawa, Canada K1G 0G8

Price per year: \$75.00 + G.S.T. - in Canada; \$97.50 (U.S.) - outside Canada.  
© Minister of National Health and Welfare 1996