ISSN 1188-4169

Canada Communicable Disease Report

FAX

Vol . 21-9

Date of publication: 15 May 1995

Contained in this FAX issue: *(No. of pages: 5)*

Update

HANTAVIRUS PULMONARY SYNDROME IN CANADA

The first recognized Canadian cases of hantavirus pulmonary syndrome (HPS) occurred in British Columbia in 1994[1]. We report four additional laboratory-confirmed cases diagnosed in Alberta, three occurred in October 1994 and one in June 1990.

Case 1

A 58-year-old married car salesmen was initially diagnosed with gastroenteritis when he presented to a local hospital emergency department with fever, chills, nausea, vomiting, and diarrhea. He was admitted to hospital the following day with a diagnosis of pneumonia. Due to his rapidly deteriorating condition, he was transferred the next day to a tertiary care hospital. On admission to the intensive care unit (ICU) he was in respiratory failure. He received over 24 litres of intravenous (IV) fluids and was treated with broad spectrum antibiotics, inotropes, and plasma volume expanders. He died about 30 hours after admission. Limited autopsy dissection was performed to collect fresh liver tissue.

Case 2

A 32-year-old farmer was admitted to a local hospital with pyrexia of uncertain origin when he presented to the emergency department with fever, myalgias, nausea, and vomiting. Two days later he was transferred to a tertiary care hospital with atypical pneumonia and increasing respiratory compromise. He was mechanically ventilated in the ICU and received antibiotics, steroids, inotropes, and ribavirin. He recovered and was discharged home after 16 days of hospitalization.

Case 3

A 42-year-old farmer with a history of hypertension was admitted to a local hospital with fever, headache, and shortness of breath. He confessed to discontinuing his antihypertensive medication 8 months prior to admission. His clinical presentation included fever, hypertension, respiratory compromise, and proteinuria. He was treated with antibiotics and anti-hypertensive medication and received oxygen by mask. After 8 days he was transferred to a tertiary care hospital for assessment of renal dysfunction and pneumonitis. He was discharged 5 days later after his blood pressure was controlled and his respiratory symptoms had resolved. Although the diagnosis of HPS was initially suspected, serology was not requested. Diagnosis was later confirmed from stored serum.

Case 4

This case was retrospectively diagnosed with HPS. As a 42-year-old army officer, he developed a febrile illness with myalgias, nausea, vomiting, and shortness of breath during military training manoeuvres in 1990. He became seriously ill and was transferred to a tertiary care hospital where he was mechanically ventilated, experienced numerous complications, and survived.

Discussion

A summary of the Canadian experience to date is presented. All seven cases presented with symptoms of flu-like illness and were hospitalized. During the course of their illnesses, all cases had bilateral pulmonary infiltrates on chest x-ray and thrombocytopenia. They all developed a systemic inflammatory response syndrome defined by at least two of the following: temperature $> 38^{o}$ C or $< 36^{o}$ C, tachycardia > 90 beats per minute, tachypnea (respiratory rate ≥ 20 breaths per minute or $PaCO_2 < 32$ mm Hg), and alterations in white blood cell counts ($> 12.0 \times 10^9$/L, $< 4.0 \times 10^9$/L, or > 10% band forms)[2]. Diagnoses were confirmed by serology, immunohistochemistry, or polymerase chain reaction (PCR) studies. The average age was 40.6 years (range: 31 to 58 years). One case was female. Mortality was 29% with one death in each province. Two of the five cases who were mechanically ventilated died. Two cases did not develop severe respiratory

compromise and required only oxygen supplementation. Of the five surviving cases, one developed hypertension during recuperation from his illness and another one has permanent hearing loss probably as a result of aminoglycoside toxicity and also has decreased total lung and oxygen diffusion capacity.

All cases had a history of rodent exposure, including deer mice. The intensity of exposures varied greatly. At the one extreme, a case had disposed of a single mouse caught in a trap. At the other extreme, a case had handled and inspected up to 600 live mice in a period of 1 month. Four cases were most likely exposed during occupational activities. Exposure histories support an incubation period of 6 to 42 days, similar to other hantaviruses known to cause hemorrhagic fever with renal syndrome[3].

Twenty-three family members and co-workers of the 1994 cases had blood taken. None showed any serologic evidence of hantavirus infection.

All cases occurred in areas characterized by grasslands and dry climate — the Bunchgrass biogeoclimatic zone in British Columbia and Aspen parkland ecoregion in Alberta.

Rodents from the areas of the British Columbia cases reported earlier[1] and from the Alberta cases reported here have been captured and tested for hantavirus antibodies. Seroprevalence of Sin nombre antibodies in deer mice trapped in British Columbia ranged from 3.4% to 20.8% and in Alberta from 1.2% to 19.6%.

Acknowledgements

We would like to thank all those who contributed to the care and investigation of the Alberta cases including Dr. J. Waters, Provincial Epidemiologist; Dr. J. Preiksaitis, Provincial Laboratory; Dr. W. Moulaison, Department of National Defense; Drs. L. Boychuk, D. Callaghan and W. Dickout, Misericordia Hospital; Drs. W. Chin, M. Joffe, L. Miedzinski, and G. Sheehan, University of Alberta Hospital; Dr. M. Savard, Stony Plain Municipal Hospital; Dr. H. Murray, Wainright and District Health Care Complex; Dr. I. Ferguson, Royal Alexander Hospital; Dr. E. York, Wetaskiwin General Hospital; and the staff of Stony Plain - Lac Ste-Anne and Minburn-Vermillion Health Units.

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Source: *DH Werker, MD, Federal Field Epidemiologist, BC Centre for Disease Control, Vancouver; AE Singh, MD, Infectious Diseases, University of Alberta Hospitals, Edmonton; H Artsob, PhD, National Laboratory for Special Pathogens; and J Hockin, MD, Field Epidemiology Division, LCDC, Ottawa.*

Editorial Comment

Hantavirus pulmonary syndrome (HPS), first described in the United States in 1993, is an emerging infectious disease associated with high morbidity and mortality. Among 103 cases identified in 21 states as of 1 February, 1995, the case-fatality rate has been 52.4% with a mean age of 35.0 years (range: 11 to 69 years) (CDC, unpublished data). The earliest retrospective case occurred in 1959[1]. However, traditional knowledge of the Navajo Nation suggests this disease has been in existence longer. Infection in humans occurs primarily through exposure to aerosolized Sin nombre virus (previously named Muerto canyon virus) from excreta of infected rodents. Deer mice (*Peromyscus maniculatus*) are the principal reservoir[2].

Initial Canadian experience indicates that HPS is similar to that described in the U.S. Because the deer mouse is found in most of Canada, further cases can be expected. Deer mice have tested positive to Sin nombre antibodies in Saskatchewan, Manitoba and Ontario, as well as Alberta and British Columbia.

In British Columbia there was no evidence of traditional knowledge or mythology about HPS among the Native populations historically inhabiting the areas where cases occurred (R. Bouchard, Consultant B.C. Indian Language Project: personal communication, 1995).

There are no pathognomonic clinical signs and symptoms nor rapid diagnostic tests that assist in diagnosing HPS. When HPS is suspected, patient outcome is likely to improve with timely transfer to a facility with capacity for critical care monitoring[3]. Meticulous maintenance of proper fluid balance and oxygenation and inotropic support are life-saving. There are currently no medications with proven efficacy against HPS. An investigational open-label trial of intravenous ribavirin conducted in the U.S. showed no clear positive influence on outcome; the trial has since been terminated[4].

When an unexplained respiratory illness results in death, HPS may be confirmed by an autopsy examination demonstrating noncardiogenic pulmonary edema without an identifiable specific cause of death and positive serology, immunohistochemistry, or PCR[5]. No occupational disease or infection from hantaviruses has been reported as a result of examining autopsy specimens. It is recommended that personnel conducting autopsy examinations on suspected hantavirus cases observe universal precautions, protect mucous membranes, and use respiratory protection for aerosol-generating procedures[6].

The temporal association of hypertension with HPS has not been previously reported although hypertensive renal disease has been associated with other hantaviruses[7].

Current experience with Sin nombre virus indicates that asymptomatic infection is rare. In the U.S., serologic testing on contacts of HPS cases has identified only 10 people with positive Sin nombre antibody titres without any apparent history of disease (Dr. L. Armstrong, Centers for Disease Control and Prevention: personal communication, 1995).

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PRELIMINARY REPORT: COMPARATIVE EVALUATION OF THE EFFECTIVENESS OF GAS STERILIZERS

Introduction

Sterilization of temperature-sensitive items has traditionally involved gas sterilizers that used ethylene oxide as the sterilant and freon (a chlorofluorocarbon) as the carrier gas. The gas mixture used in these sterilizers consists of 12% ethylene oxide and 88% freon and the units were referred to as 12/88 sterilizers. The recent legislation banning the sale of chlorofluorocarbons (CFCs) in Canada, which will be effective 1 January, 1996, has resulted in hospitals actively seeking alternatives to the 12/88 ethylene oxide sterilizers. Some of the existing alternative sterilizers include 100% ethylene oxide models (no freon carrier gas) and "plasma"-based types. The plasma sterilizers operate at low temperatures and use hydrogen peroxide (H_2O_2) or peracetic acid, which is exposed to a strong electric or magnetic field to produce a plasma of reactive particles that kills microorganisms. These sterilizers have short turnaround times (75 minutes to 3 hours) compared to the ethylene oxide types, with turnaround times of 18 to 24 hours. There have been few independent evaluations of these new technology plasma sterilizers[1-6]. This report presents the preliminary findings of a comparative study that assessed the effectiveness of the existing 12/88 sterilizer, 100% ethylene oxide sterilizers (manufactured by AMSCO and 3M), the VHP rigid scope plasma sterilizer (AMSCO), the STERRAD H_2O_2 plasma sterilizer (Johnson & Johnson), and the ABTOX peracetic acid plasma sterilizer (represented by Ingram and Bell in Canada).

The Study

There were two phases to the study: 1) surface sterilization of bacteria in the absence of additional serum and salt, and 2) surface and narrow lumen sterilization of bacteria in medium containing 10% serum and 0.65% salt. Surface sterilization involved bacteria inoculated onto porcelain penicylinders; lumen sterilization consisted of bacteria inoculated at the midpoint inside a piece of flexible plastic tubing 125 cm long with a 3.2 mm internal lumen. The organisms tested consisted of *Enterococcus faecalis, Escherichia coli, Pseudomonas aeruginosa, Mycobacterium chelonei, Bacillus sterothermophilus, B. subtilis and B. circulans.* Individual replicate carriers were inoculated with a 10^6 colony-forming unit (cfu) of each organism tested. The inoculated carriers were dried overnight, wrapped in disposable wraps and processed in the various sterilizers. For the VHP rigid scope sterilizer, the bacteria were inoculated onto stainless steel penicylinders and inserted inside a stainless steel rod to mimic a rigid scope.

Results

Phase 1

In the absence of serum and salt, all six sterilizers could effect complete sterility for the organisms tested (*E. faecalis, B. sterothermophilus, B. subtilis*) when inoculated onto porcelain penicylinders. This represented a 6 LOG_{10} reduction in the bacterial load.

Phase 2

In the presence of 10% serum and 0.65% salt, only the 12/88 sterilizer could consistently sterilize 97% of the inoculated penicylinder carriers (Table 1). The additional challenge of 10% serum and 0.65% salt resulted in decreased killing ability for the 100% ethylene oxide sterilizers as well as the two plasma sterilizers (Table 1). All sterilizers could effect a 6 LOG_{10} reduction for *E. coli* and *P. aeruginosa*; however, only a 2 to 5 LOG_{10} reduction was achieved for the *Bacillus* strains or the *E. faecalis*. The plasma sterilizers had some penicylinders that had low levels of *M. chelonei* remaining after processing, whereas the 100% ethylene oxide sterilizers achieved sterility for all penicylinders inoculated with this organism.

The interference due to serum and salt was even more pronounced when the carrier was a narrow lumen (Table 1). Even the 12/88 was only able to achieve sterility in 44% of the inoculated lumen carriers. The results of the other sterilizers tested were even less favourable, ranging from 6% to 35% (Table 1). The 12/88 sterilizer, both of the 100% ethylene oxide sterilizers and the STERRAD sterilizer were able to produce a 6 LOG_{10} reduction in *E. coli* and *P. aeruginosa* but could only achieve a 2 to 5 LOG_{10} reduction in *E. faecalis*, *M. chelonei*, and the three bacillus species tested. The STERRAD system uses a lumen adaptor to improve delivery of H_2O_2 inside the lumen and this appeared to enhance its ability to kill organisms making it equivalent to the 12/88 sterilizer and the 100% ethylene oxide sterilizers (Table 1). However, none of the sterilizers could effectively eradicate organisms from within a narrow lumen when the additional challenge of 10% serum and 0.65% salt was present.

Conclusions

All of the non-CFC-based sterilizers tested were equivalent to the existing 12/88 ethylene oxide sterilizer if the items seeded with bacteria were free of additional protein and salt. However, surface sterilization was severely hampered in the 100% ethylene oxide and plasma sterilizers compared to the 12/88 one when bacteria were in the presence of serum and salt, surrogates for an inadequately cleaned instrument. The margin of safety for the non-CFC-based sterilizers is less than that of the 12/88 sterilizers. The interference caused by serum and salt was even more pronounced when lumens were used as carriers. Even the existing 12/88 ethylene oxide sterilizer was ineffective when the bacteria were suspended in serum and salt within a narrow lumen (3.2 mm internal diameter) tubing that was 125 cm long (similar dimensions to a flexible ERCP endoscope).

The differences observed between the 12/88 sterilizer and the 100% ethylene oxide sterilizers are likely due to the longer exposure time (1 hour 45 minutes) for the 12/88 sterilizer compared to the 1-hour exposure time for the 100% ethylene oxide sterilizers.

Table 1
Ability of sterilizers to completely sterilize inoculated carriers in the presence of serum and salt*

Type of Sterilization	Type of Sterilizer					
	Current 12/88 ethylene oxide	AMSCO 100% ethylene oxide	3M 100% ethylene oxide	ABTOX peracetic acid plasma	STERRAD H_2O_2 plasma	AMSCO rigid scope plasma
SURFACE number sterile/ number tested (% sterile) (all organisms)	61/63 (97%)	49/63 (78%)	31/63 (49%)	20/63 (32%)	23/63 (37%)	19/54 (35%)
LUMEN number sterile/number tested (% sterile) (all organisms)	28/63 (44%)	21/63 (33%)	18/63 (29%)	4/63 (6%)	22/63 (35%)	N/A/S/O

* All bacteria were suspended in RPMI (tissue culture medium) containing 10% serum and 0.65% salt; approximately a 10^9 cfu/carrier was seeded onto each carrier and allowed to dry. After sterilization, the carrier was placed into broth medium and incubated for 5 days (10 days for *M. chelonei*). If no growth occurred, the carrier was considered to be sterile. The organisms were tested in triplicate on three separate days giving a total of 9 replicates for each bacterium.
NA - Not applicable

These results emphasize that it is CRITICAL for items intended for sterilization in the plasma or 100% ethylene oxide sterilizers to be METICULOUSLY cleaned prior to sterilizing. The current practise of sterilizing flexible endoscopes in ethylene oxide appears to be suboptimal if body fluids and salt remain within the lumen. More studies are needed to define how these instruments can be most effectively sterilized since none of the new (non-CFC-based) sterilizers are any more effective at sterilizing long narrow lumens under conditions where serum and salt may be present than the existing 12/88 ethylene oxide type.

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Source: *Michelle J Alfa, PhD, SCM (CCM), Assistant Director, Microbiology, St. Boniface General Hospital, Winnipeg, Manitoba.*

Editorial Comment

CFCs have been used for many years as inflammability suppressants for ethylene oxide (EtO) used in sterilization of medical devices (12/88 sterilant). The deadline for the cessation of the sale of CFCs is 1 January, 1996, and hence the sale of the 12/88 sterilant gas. Health care facilities are facing difficult choices as they search for an effective replacement for sterilizers that use 12/88 gas.

Technologies that do not use CFCs in the sterilant are available on the Canadian market. However, there is little objective information in the literature to evaluate the efficacy of the sterilants and their associated technologies. Dr. Alfa's study of the comparative efficacy of some of the available replacements to the 12/88 sterilizers is most welcome.

While all of the non-CFC-based sterilizers tested were equivalent to the existing 12/88 sterilizer when clear of protein and salt, the failure of 100% EtO and the plasma sterilizers highlights an ongoing problem and re-emphasizes the importance of meticulous cleaning of all items prior to sterilization. The reduced margin of safety for the 100% EtO and the plasma sterilizers presents a continuing challenge as many of the complex instruments used in surgery today are extremely difficult to disassemble and clean effectively.

Dr. Alfa's description of the inefficacy of all the sterilants, when challenged by narrow lumen tubing, must cause concern to all those using endoscopes and other such flexible scopes in their practice. Practitioners who clean these instruments know that it is almost impossible to clean many of the tiny lumens in flexible scopes. Further studies are urgently needed to improve the design of flexible scopes to enable effective cleaning and sterilization of these instruments.

In 1994 the Canadian Hospital Association established a national task force to examine the issue of alternatives to 12/88 EtO sterilization. The report entitled "Elimination of CFCs in Health Care Facilities" contains a decision-making framework to assist health care facilities in addressing the wide range of issues related to the purchase and use of alternative sterilizers. This document can be obtained from the **Canadian Hospital Association, 17 York Street, Suite 100, Ottawa, Ontario, K1N 9J6 (Cost: $35).**

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IODINE AND HEALTH

Eliminating Iodine Deficiency Disorders Safely Through Salt Iodization

A statement by the World Health Organization

Iodine deficiency disorders (IDD) are both easy and inexpensive to prevent, yet they continue to be a significant public health problem in 118 countries. An estimated 1,571 million people worldwide live in iodine-deficient environments and are thus at risk of IDD; 20 million of these are believed to be significantly mentally handicapped as a result. A large proportion of the severely deficient are women in their reproductive years whose babies are at high risk of irreversible mental retardation unless they receive adequate amounts of iodine.

Despite the endorsement of universal salt iodization in numerous international forums as an effective means of preventive IDD, queries are still made about the safety of providing iodized salt to non-deficient populations. In response to concerns expressed, and to facilitate decision making by responsible authorities, WHO has issued a statement that summarizes the cumulative evidence in this regard.

Free copies of this statement (document WHO/NUT/94.4) are available in English and French (Spanish version in preparation) from the **Nutrition Unit, WHO, 1211 Geneva 27, Switzerland**.

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

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