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National Advisory Committee on Immunization (NACI)*
SUPPLEMENTARY STATEMENT ON HEPATITIS A PREVENTION

In a recent statement on the prevention of infections caused by hepatitis A virus (HAV), NACI[1] described the usual indications for use of immune serum globulin (IG) and the newly available inactivated hepatitis A vaccine (HAVRIX™, SmithKline Beecham). Subsequently, a more potent vaccine formulation was licensed, permitting a single dose primary immunization of adults. This supplementary statement addresses this development and comments on vaccine use in children.

New Vaccine Formulation for Adults

When inactivated hepatitis A vaccine (HAVRIX™, SmithKline Beecham) was first licensed in Canada, the formulation for adults contained 720 enzyme-linked immunosorbent assay (ELISA) units (ELU) of viral antigen in 1.0 mL, to be administered as a three-dose series (at 0, 1 and 6 to 12 months)[1]. The new formulation contains 1,440 ELU per 1.0 mL dose, to be administered as a single primary dose. In studies of healthy adults[2], 88% had serum antibody against HAV measurable by ELISA 2 weeks after receiving a 1,440 ELU primary dose and 99% seroconverted after 4 weeks. Virus neutralizing antibody, a better indicator of protection, was present in 94% 4 weeks post-immunization[2] but is not consistently present until that time. Current data for HAVRIX™[2] indicate that antibodies will persist for at least 1 year in most individuals following the single primary dose. A booster dose may be administered at any time between 6 and 12 months after the primary dose, to induce long-term persistence. A satisfactory booster dose response can be achieved using a dose of either 720 or 1,440 ELU. Kinetic models of antibody decline suggest that protective levels of anti-HAV could persist for at least 20 years[2].

The two formulations differ little in the frequency of adverse reactions. Local adverse reactions are most likely to result from the alum adjuvant, the concentration of which does not differ between the 720 and 1,440 ELU formulations. Both are preserved with 2-phenoxyethanol and contain the same concentrations of trace ingredients. In pre-licensure studies[2], injection site soreness was reported after half the vaccinations with 1,440 ELU but was usually mild. Induration, redness or swelling are reported after 4% to 7% of vaccinations. Systemic adverse events were similar for the HAVRIX™ formulations with headache being the most frequently reported symptom (about 14% of vaccinations), followed by malaise (7%).

HAVRIX™ 1,440 can be given concurrently with IG, at separate injection sites, for persons needing rapid protection, i.e., whose exposure will begin within 4 weeks of vaccination.

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HAVRIX™ 1,440 is not recommended for children.

The particular advantages of the new formulations are 1) a simplified, one-dose primary immunization course, 2) a shorter interval between vaccination and induction of protective antibody responses against HAV in most individuals (about 4 weeks), and 3) reduced cost of primary immunization. The new formulation will be more convenient for travellers needing protection prior to entering HAV-endemic areas and will be better suited for use in controlling outbreaks (an application that is still considered investigational). Vaccine use in outbreaks should only be considered after discussion with public health officials.

Vaccine Use in Children

HAVRIX™ is not yet licensed for children in Canada and no specific pediatric formulation is available. In the United States, licensure includes use in children 2 to 18 years of age, for whom a dosage of 360 ELU is recommended, in a schedule of 0, 1 and 6 to 12 months[3]. The U.S. licensure provisions reflect a more up-to-date application than was available in Canada. It is likely that licensure in Canada will be updated to coincide with that in the U.S. In anticipation of that approval, Canadian children who would benefit from HAV vaccine[1] should be offered it if they fall into one of the categories for which it is recommended. The appropriate dose (360 ELU) is more readily achieved by splitting a vial containing 720 ELU in 1.0 mL than one with 1,440 ELU in 0.1 mL.

In general, children respond well to HAV vaccine, with over 90% developing antibody within 4 weeks of receiving the first dose[2,6]. Use of a larger initial dose (720 ELU) to elicit protection in children with one vaccination is being evaluated but no recommendation can be made at this time.

Limited data are available on vaccine use in children younger than 24 months[4] but they raise no special concerns regarding vaccine safety. Infants with maternally-derived antibody to HAV may have blunted responses to HAV vaccine, analogous to adults given IG and vaccine concurrently[5]. The dosage for children of all ages is 360 ELU, in a schedule of 0, 1 and 6 to 12 months.

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International Notes

ARBOVIRUS SURVEILLANCE — UNITED STATES

Arboviruses are mosquito-borne and tick-borne agents that persist in nature in complex cycles involving birds and mammals, including humans. Characteristics of arboviral infection include fever, headache, encephalitis, and sometimes cause death. In 1994, health departments in 20 states reported 100 presumptive or confirmed human cases of arboviral disease* to the Centers for Disease Control and Prevention (CDC). Of these, 76 were California (CAL) serogroup encephalitis; 20, Saint Louis encephalitis (SLE); 2, western equine encephalomyelitis (WEE); 1, eastern equine encephalomyelitis (EEE); and 1, Powassan encephalitis (POW).

California serogroup encephalitis

During 1994, a total of 76 human CAL serogroup encephalitis cases were reported from 13 states: West Virginia (32 cases), Ohio (14), Wisconsin (7), Illinois (6), Minnesota (4), Indiana and North Carolina (3 each), Alabama (2), and Iowa, Kentucky, Michigan, Rhode Island, and Virginia (1 each). Patients ranged in age from 6 months to 26 years (mean: 7 years). A total of 57 cases (75%) occurred among males. Onset of illness occurred in May (1 case), June (1), July (12), August (35), September (22), and October (5).

Saint Louis encephalitis

During 1994, a total of 20 human cases of SLE were reported from five states. Sixteen cases were reported in Louisiana; most of them (14) occurred in urban New Orleans. Three cases (in 44- and 60-year-old men and a 63-year-old woman) were fatal. Patients ranged in age from 12 to 78 years (mean: 46 years). Of the 16 cases, nine occurred among males. SLE cases were also reported in residents of California, Florida, Mississippi, and Texas (1 each). For the 20 total cases, onsets of illness occurred in July (1 case), August (9), September (9), and October (1).

Western and eastern equine encephalomyelitis

During 1994, two human cases of WEE were reported from Wyoming in a 40-year-old woman and a 42-year-old man. One

* At CDC, a confirmed case is defined as febrile illness with mild neurologic symptoms, aseptic meningitis, or encephalitis with onset during a period when arbovirus transmission is likely to occur, plus at least 1 of the following criteria: (1) four-fold or greater rise in serum antibody titre, (2) viral isolation from tissue, blood, or cerebrospinal fluid; or (3) specific immunoglobulin M (IgM) antibody in cerebrospinal fluid. A presumptive case is defined as compatible illness, plus either a stable elevated antibody titre to an arbovirus (≥ 320 by hemagglutination inhibition, ≥ 128 by complement fixation, ≥ 256 by immunofluorescent assay, or ≥ 160 by plaque-reduction neutralization test) or specific IgM antibody in serum by enzyme immunoassay.

human case of EEE in a 67-year-old man was reported from Louisiana.

Powassan encephalitis

POW was serologically confirmed in a 49-year-old female resident of Massachussetts who had onset of illness on 24 May. She reported removing an engorged tick from her abdomen approximately 2 weeks before onset of symptoms. She was admitted to hospital on 25 May with a diagnosis of meningo-encephalitis, which progressed during the following 72 hours to encephalitis involving the brain stem and basal ganglia. During hospitalization, the patient was comatose for 3 days and required mechanical ventilation. On examination in August 1995, she had residual weakness in her right leg requiring a brace. The patient's prolonged convalescence is consistent with that reported for POW encephalitis.

MMWR Editorial Note: CAL serogroup encephalitis remains the most frequently reported arbovirus infection in the United States. Although the number of these cases has remained relatively constant since the 1970s and was reported primarily from the Midwest, the number of cases reported from the South has increased.

In general, SLE occurs as periodic focal outbreaks followed by years of sporadic cases. In 1994, a small focal outbreak of SLE occurred in urban New Orleans. Evaluation of patients by date of illness onset and location suggests that the earliest cases occurred among persons living within or in proximity to urban public housing projects. Subsequent cases followed a pattern of radial spread from the central urban area, although the small number of cases preclude a definitive analysis. Large populations of immature and adult *Cules pipiens quinquefasciatus* mosquitos have been found under housing units. Leaking sewer lines beneath these housing units provided an extensive and ideal habitat for the SLE virus vector mosquito.

POW virus, a tick-borne flavivirus most closely related to Russian spring-summer and Central European encephalitis viruses, appears to be widely distributed in the United States. In North America, *Ixodes cookei* has been implicated as the principal tick vector, and the virus has been recovered from several rodent and carnivore species**.

Based on evaluation of the 24 total POW cases that occurred in North America during 1958-1994, risk for infection may be highest in wooded areas where potential contact with infected rodent or carnivore hosts or tick vectors is greatest. Of the 24 cases, 21 occurred in persons aged < 20 years. Four of the acute infections were fatal, and two patients died 1 and 3 years after onset as a result of sequelae reported to be directly related to the disease.

Health-care providers should consider arboviruses in the differential diagnosis of aseptic meningitis and encephalitis cases during the summer months. Serum (acute and convalescent) and cerebrospinal fluid samples should be obtained for serologic testing, and cases should be promptly reported. New rapid diagnostic techniques, including detection of IgM antibody in acute serum or cerebrospinal fluids, have facilitated confirmation of arbovirus infections.

Source: *WHO Weekly Epidemiological Record, Vol 70, No 46, 1995.*

INFLUENZA SURVEILLANCE WORLDWIDE

Belgium (12 November, 1995): Influenza A was diagnosed in two sporadic cases in the northern and southern parts of the country in the first week of November.

Chile (6 November, 1995): The outbreaks in Santiago were over by mid-September 1995, but cases of influenza A continued to be detected in other parts of the country during September and October. All influenza A cases further identified were of H_3N_2 subtype.

Germany (15 November, 1995): Influenza A has been diagnosed in two sporadic cases in the southern part of the country. One was confirmed by isolation and further identified as influenza A(H_3N_2). Sentinel physicians participating in influenza surveillance reported acute respiratory infections in 10.8% of their patients in the second week of November, which is slightly more than expected. Some regions reported a marked increase in respiratory tract infections and work absenteeism during November.

Norway (21 November, 1995): Influenza A(H_3N_2) virus was isolated from a patient in Oslo in the week ending 19 November. A few counties have reported influenza morbidity rates exceeding 100 per 100,000 population, but the overall rate for the country is below this figure.

Portugal (16 November, 1995): The incidence of influenza-like illness has increased since mid-October and reached 38.3 per 100,000 population in the week ending 12 November. Since the beginning of October, influenza A has been diagnosed in 18 cases; most have occurred since mid-October.

** *Tamiasciurus hudsonicus, Marmota monax* and *Mephitis mephitis, Spilogale putorius, Vulpes* sp. *Urocyon cinereoargenteus* (grey fox), *Mustella erminea* and Mustella frenata, and *Peromyscus maniculatus*.

Spain (25 November, 1995): Influenza A has been diagnosed in two patients with influenza-like illness in the Provinces of Soria and Valladolid in the central-northern part of the country.

Switzerland (14 November, 1995): Influenza A(H_1N_1) virus has been isolated from a sporadic case in a 37-year-old man from the central part of the country. The percentage of patients with influenza-like illness seen by sentinel physicians was low in October and during the first week of November.

United Kingdom (28 November, 1995): Indices of clinical influenza activity increased markedly and outbreaks continued to be reported in schools and homes for the elderly during November. Over 140 cases have been confirmed by virus isolation and investigated centrally. Except for one influenza A virus of H_1N_1 subtype, all have been influenza A(H_3N_2) viruses, similar to the variant recommended for inclusion in this season's influenza vaccine, A/Johannesburg/33/94(H_3N_2).

United States of America (3 November, 1995): Influenza activity was low during October. By the end of the month influenza viruses had been isolated from sporadic cases in 10 states: influenza A(H_1N_1) in Arizona, New York and Texas, influenza A(H_3N_2) in Oklahoma, influenza A not further typed in Colorado, Idaho, Montana, New York and Washington, and influenza B in California and Utah.

Source: *WHO Weekly Epidemiological Record, Vol 70, Nos 46, 47 and 48, 1995.*

ANTIGENIC ANALYSIS OF RECENT INFLUENZA VIRUS ISOLATES AND INFLUENZA ACTIVITY IN THE SOUTHERN HEMISPHERE

Since the influenza vaccine recommendations for the 1995-1996 season were issued, influenza virus isolates from Africa, the Americas, Asia, Europe and Oceania have been characterized antigenically at the WHO Collaborating Centres.

Both influenza A(H_3N_2) and influenza B were prevalent in Asia and Europe. In North America the majority of isolates were influenza A(H_3N_2). In recent months influenza A(H_1N_1) viruses have become more prominent. Influenza activity in the southern hemisphere has been moderate. Activity due to influenza A(H_3N_2) was reported in South Africa and Zambia; influenza A(H_1N_1) was also detected in South Africa. Influenza B was predominant in New Zealand and outbreaks in Australia were due principally to influenza A(H_1N_1) viruses. In South American countries (Argentina, Brazil and Chile) activity was due to both influenza A(H_3N_2) and influenza B viruses.

Antigenically the majority of influenza viruses isolated were closely related to the recommended vaccine strains. The majority of influenza A(H_3N_2) isolates were similar to A/Johannesburg/33/94. Most influenza B viruses were similar to B/Beijing/184/93. Some heterogenicity has been seen among the influenza A(H_1N_1) viruses; the majority was similar to A/Singapore/6/86, A/Victoria/36/88 and A/Texas/36/91.

Source: *WHO Weekly Epidemiological Record, Vol 70, No 39, 1995.*

Notifiable Diseases Summary

We have excluded this table from the FAX issue of Canada Communicable Disease Report for those readers who do not need this information. For those readers interested in this table, call the FAX line and select the index to get the access number.

Notifiable Diseases Summaries published to date in this new format (FAX) can be found in the index under the same name.

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