EPIDEMIOLOGY SECTION

Connecticut Epidemiologist

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Douglas S. Lloyd, M.D., M.P.H., Commissioner

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UPDATE ON HEMORRHAGIC COLITIS

Since the investigation of outbreaks of hemorrhagic colitis in Oregon and Michigan (1), the Enteric Diseases Branch, Division of Bacterial Diseases at the Centers for Disease Control (CDC) has implemented a program to evaluate and characterize sporadic cases of the illness occurring in the United States.

Clinical Description

Hemorrhagic colitis is a newly recognized diarrheal illness associated with a rare serotype of E. coli 0157:H7 (2). The disease is characterized by severe generalized or right lower quadrant crampy abdominal pain, and watery diarrhea followed by grossly bloody diarrhea resembling a lower gastrointestinal bleed. Absence of fever or low grade fever ($\leq$38.5C) has been noted.

Some patients may exhibit rebound tenderness or guarding on abdominal examination. Leucocyte counts range from 7,600 to 19,000 with a minimal or moderate shift to the left. Barium enema radiographs typically show edema of the ascending or transverse colon, whereas the sigmoidoscopic studies show either normal or hyperemic mucosa. Stool cultures are negative for Salmonella, Shigella, Campylobacter, Yersinia, and ova and parasites.

Approximately 75% of cases have been hospitalized; average duration of illness was 4-5 days with a range of 2 to 10 days. All hospitalized patients have required intravenous fluids, but no one has required a blood transfusion. Some have received parenteral or oral antibiotics. Despite the severe initial clinical presentation, the illness appears to be self-limited. No complications, sequelae, or deaths have been reported.

The pathophysiology of hemorrhagic colitis is unknown. The Canadian Laboratory Centers for Disease Control (LCDC) demonstrated that the E. coli 0157:H7 isolates from the Canadian outbreak did not produce heat-labile or heat-stable enterotoxin and were not invasive. However, they did produce a cytotoxin in the Vero cell tissue culture assay (5). Further work is necessary to show that this cytotoxin plays a role in pathogenesis.

Outbreaks and Case Studies

Two outbreaks of this disease involving about 47 cases occurred in Oregon and Michigan in the first half of 1982. Illnesses were associated with eating hamburgers. E. coli 0157:H7 was isolated from stool specimens from 9 of 12 cases of hemorrhagic colitis who were cultured within four days of onset of illness. This E. coli serotype was not isolated from control subjects and has been identified only once among $>$ 3,000 E. coli isolates submitted to the CDC for serotyping since 1973. That isolate was recovered from a California woman who had an acute, self-limited, afebrile illness with severe abdominal cramps and grossly bloody diarrhea. This unusual serotype was also isolated from a frozen, raw hamburger patty from a lot used by an implicated fast-food chain in Michigan.

A third outbreak which occurred at a home for the aged in Ottawa, Ontario, Canada, has now been reported (3,4). E. coli 0157:H7 was isolated from over half of the cases. A single lot of hamburger prepared in the home's kitchen and served repeatedly over a fifteen day period was considered the most likely vehicle for transmission of the disease.

In addition, since surveillance for sporadic cases of hemorrhagic colitis began in August 1982, 39 cases meeting the CDC's criteria have been reported from 18 states. E. coli 0157:H7 has been isolated from 6 of 21 stool specimens from these patients.

These reports have further defined the clinical and epidemiologic features of hemorrhagic colitis and support the hypothesis that E. coli 0157:H7 is a cause of hemorrhagic colitis.

Surveillance

Connecticut's Epidemiology Section is participating in this CDC study and would appreciate your assistance. We ask that suspect cases that fulfill the criteria of 1) abdominal cramps, 2) grossly bloody diarrhea, 3) absent or low grade fever, and 4) stool specimens negative for parasites and enteric pathogens be reported to the Epidemiology Program (Pat Checko or Lori Amsterdam) at (203) 566-5058.

Potential cases meeting the case definition will be interviewed utilizing the CDC case report questionnaire. As part of the epidemiologic investigation, a neighborhood control named by the case will also be interviewed.

The epidemiology staff, in conjunction with state laboratory personnel, will coordinate arrangements for collection and transport of stool, sera, and food specimens as well as E. coli isolates. Appropriate specimens and/or isolates from suspected cases will be submitted to the CDC for serotyping. All isolates of E. coli 0157:H7 will be subjected to plasmid profile analysis.

Microbiologic Studies

Stool cultures should be collected within 4 days of onset of illness and prior to antibiotic therapy. Serial stool specimens collected from affected residents in the Canadian outbreak were positive up to 11 days after onset (4).

The laboratory should plate the specimen on MacConkey agar as part of the primary isolation, and the remaining stool should be frozen without preservative at -70°C. Minimally, laboratory testing should rule out Salmonella, Shigella, and Campylobacter as potential etiologic agents. If no other pathogens are present, at least 10 colonies from MacConkey should be subcultured to slants. The isolates and frozen stools should be sent to the Enteric Disease Laboratory of the State Laboratory, where the isolates will be tested for sorbitol activity, prior to submission to CDC. (CDC will not accept specimens for E. coli serotyping submitted directly from laboratories in Connecticut.)

Questions regarding appropriate culturing techniques and referral of isolates to Atlanta should be directed to the Enteric Diseases Laboratory (Arthur Bruce, 203-566-4340).

Acute and convalescent sera should also be collected on individuals who meet the case definition. The acute serum should be frozen at -70°C and held until the convalescent serum has been drawn (3-4 weeks following collection of the acute serum).

1. Riley LW, Remis RS, Helgerson SD, et al. Outbreaks of hemorrhagic colitis associated with a rare Escherichia coli serotype. N Engl J Med 1983; 308:681-685.

2. CDC. Isolation of E. coli 0157:H7 from sporadic cases of hemorrhagic colitis. United States. MMWR 1982; 31:580, 585.

3. Canada Diseases Weekly Report 1983; 9:29-32.

4. CDC. Outbreak of hemorrhagic colitis, Ottawa, Canada, MMWR 1983; 32:133-134.

5. Johnson WM, Lior H, Bezansom GS. Cytotoxic Escherichia coli 0157:H7 associated with haemorrhagic colitis in Canada. Lancet 1983; 1:76.

THE SAFETY OF HEPATITIS B VACCINE

Since its licensure in 1981 and its general availablity in July 1982, hepatitis B virus vaccine (HBV) has been administered to over 200,000 individuals, most of whom are health care workers. Surveillance for possible vaccine related side-effects and illnesses has been initiated by the Centers for Disease Control, the Food and Drug Adminis-

tration, and Merck, Sharp, and Dohme. All illnesses reported to any of these sources have been recorded. Reports of serious illness have been followed up by telephone or personal interviews.

As of April 11, 1983, 163 complaints had been reported. Of these reports, 61 (37.4%) were considered not likely to be attributable to vaccine use because: 1) another specific cause of the complaint was identified, 2) onset of illness occurred before receipt of vaccine, or 3) the reported event was unrelated to the vaccine (e.g., deltoid pain after gluteal injection). Many of the remaining 102 illnesses may represent "background" disease rather than adverse vaccine reactions. Most involved the following sites: liver, skin, central-nervous system, and joints. About one third of all reports were minor complaints such as nausea, lethargy, or injection-site pain.

Eight of the liver-associated complaints were documented hepatitis B virus infection. Time intervals suggest that these individuals were probably already incubating the disease at the time they received the vaccine. Five other hepatitis-like illnesses involved elevation of liver enzymes with no identified cause.

Twelve individuals (7.4%) had a serious illness. Illness was defined as serious if it caused hospitalization or other intensive care, had duration of 14 days or more, caused permanent disability or a life-threatening illness. Seven of these twelve developed neurologic conditions as follows: aseptic meningitis (1), grand mal seizures (1), optic neuritis (1), and Guillain-Barré Syndrome (3) (Table 1).

It is estimated that the background rate for Guillain-Barré Syndrome (GBS) is 15 cases/million population/year. If 250,000 people were vaccinated with at least one dose, the probability of at least two cases of GBS occurring within two months is .13; the probability of at least three cases is .026. Although the latter indicates that GBS may be occurring at slightly higher than expected rates, the total number of vaccinees and GBS cases are too few to draw conclusions regarding the significance of these findings. Finally, the period between immunization and occurrence of GBS in hepatitis vaccine recipients has been 3-4 weeks, whereas influenza vaccine associated GBS cases occurred within only 1-2 weeks following immunization.

Whether acquired immune deficiency sydrome (AIDS) could be associated with HBV vaccine has been questioned, since the vaccine is made from human plasma. Since 1979, homosexual men, including those from cities with reported AIDS cases, have been the source for much of the plasma. Vaccine produced from these sources has been used in various investigative studies since 1980 and has been commercially available since 1982. To date, no AIDS in vaccine recipients has been reported outside groups with high AIDS incidence. Specifically, no AIDS cases have occurred among the several thousand individuals other than male homosexuals, (primarily health care workers), who participated in vaccine studies from 1980, to date. In addition, no cases have been reported from the over 200,000 individuals who have received HBV vaccine since its general availability in July 1982. (The latent period for AIDS, if an infectious agent

Table 1. Neurologic Diseases Reported to Hepatitis B Vaccine Surveillance Program

Type of Illness	Total # Cases	Interval After 1st Dose of Vaccine	Comments
Aseptic Meningitis	1	2 days	Recent travel history
Optic Neuritis	1		
Transverse Myelitis	1	37 days	
Grand Mal Seizure	1		
Guillain-Barré	3	4 weeks	45 y.o. male
		3 weeks	25 y.o. female; had hepatitis & CMV titers
		6 weeks	36 y.o. male; febrile illness with vomiting & diarrhea ?Enterovirus Normal nerve studies Onset after 2nd dose

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	AMEBIASIS	BOTULISM	BRUCELLOSIS	ENCEPHALITIS (TOTAL)	Primary	Post	FOODBORNE OUTBREAKS	GONORRHEA	HEPATITIS A	HEPATITIS B	HEPATITIS NON A NON B	HEPATITIS UNSPECIFIED	LEGIONELLOSIS	LEPROSY	MALARIA	MEASLES	MENINGITIS (All Types)	Aseptic	Hemophilus influenzae	Meningococcal	Other	MUMPS	PERTUSSIS	PSITTACOSIS	RABIES IN ANIMALS	REYE'S SYNDROME	ROCKY MT. SPOTTED FEVER	RUBELLA	SALMONELLA	SHIGELLA	SYPHILIS	TUBERCULOSIS (TOTAL)	Pulmonary	Other	TYPHOID FEVER
TOTAL APRIL - 1983	4	0	0	1	1	0	1	623	5	33	4	0	3	0	3	0	19	4	7	6	2	2	0	0	0	0	0	0	55	13	16	13	11	2	0
CUMULATIVE - 1983	4	0	0	4	4	0	3	2751	18	110	17	2	15	0	4	1	69	8	20	24	17	11	0	0	0	0	0	0	209	94	70	46	37	9	0
CUMULATIVE - 1982	8	1	0	12	10	2	1	2689	28	160	9	12	10	1	6	3	71	13	15	22	21	10	2	0	0	0	0	0	191	112	44	30	23	7	1

is involved, appears to be between 8 and 18 months). Two homosexual men who participated in the original HBV vaccine field trials have developed AIDS. This occurrence is not significantly different from that observed among men who were screened for participation in these trials but who were ultimately not vaccinated. Furthermore, the manufacturing process for HBV vaccine includes several procedures that inactivate representative viruses of all known types (1). Thus, both current microbiologic and empiric data provide no support for the suggestion that HBV vaccine might carry an etiologic risk for AIDS.

Surveillance for reactions that may be caused by HBV vaccine is ongoing. The vaccine is recommended for groups at risk of HBV infection (2). Health care providers are encouraged to report illness following receipt of HBV vaccine to the Epidemiology Program (566-5058). These reports will be referred to the Hepatitis Division, Center for Infectious Diseases, CDC.

References

1. CDC. Hepatitis B virus vaccine safety: report of an interagency group. MMWR 1982; 31:465-7.
2. CDC. The safety of hepatitis B virus vaccine. MMWR 1983; 32:134-136.
3. Johnson, JM. Possible side effects from the hepatitis B virus vaccine. Presented at Epidemic Intellegence Service 32nd Annual Conference, April 18-22, 1983. Centers for Disease Control, Atlanta, GA.

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