Alberta Public Health Disease Management Guidelines

Haemolytic Uremic Syndrome

Alberta

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Health.CD@gov.ab.ca

Health and Wellness Promotion Branch

Public Health and Compliance Branch

Alberta Health

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Case Definition

Confirmed Case

An acute illness diagnosed as HUS[(A)] that:

- meets the laboratory criteria[(B)]

AND

- begins within three weeks after onset of a diarrheal illness (usually bloody diarrhea), or non-diarrheal illness (less commonly), caused by an infectious organism

AND

- occurs in the absence of chronic underlying conditions that may account for renal and haematological dysfunctions

Probable Case

The following probable case definition is provided as a guideline to assist with case finding and public health management and should not be reported to Alberta Health.

An acute illness diagnosed as HUS[(A)] that:

- meets the laboratory criteria[(B)]

BUT

- without laboratory confirmation of an infectious organism causing a preceding illness

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[(A)] HUS is defined by the triad of microangiopathic haemolytic anemia, thrombocytopenia (low platelet count) and acute renal impairment. Most cases of HUS occur after an acute gastrointestinal illness (usually bloody diarrhea).

[(B)] The following are present at some time during the course of the illness (they may not all be present simultaneously):

- Acute renal impairment evidenced by elevated serum creatinine levels as follows or as determined in consultation with the attending physician:[(1)]
  - > 50 µmol/L if < 5 years of age
  - > 60 µmol/L if 5–9 years of age
  - > 90 µmol/L if 10–13 years of age
  - > 110 µmol/L if > 13 years of age
- Microangiopathic haemolytic anemia (Hb < 100g/L with fragmented red cells)
- Thrombocytopenia (< 150 x 109/L) in the absence of septicaemia, malignant hypertension, chronic uremia, collagen or vascular disorders

Reporting Requirements

Haemolytic Uremic Syndrome (HUS) is a distinct clinical syndrome that has many triggers that can be both infectious and non-infectious in nature. Typical HUS usually occurs after a prodrome of diarrhea (D^+HUS) and atypical HUS is not associated with a diarrheal prodrome (D^-HUS).

Only HUS associated with an *infectious causative organism* is reportable to Alberta Health.

Physicians, Health Practitioners and Others

Physicians, health practitioners and others shall notify the Medical Officer of Health (MOH) (or designate) of the zone, of all confirmed cases in the prescribed form by mail, fax or electronic transfer within 48 hours (two business days).

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- The MOH (or designate) of the zone where the case currently resides shall forward the initial Notifiable Disease Report (NDR) of all confirmed cases to the Chief Medical Officer of Health (CMOH) (or designate) within two weeks of notification and the final NDR (amendment) within four weeks of notification.
- For out-of-province and out-of-country reports, the following information should be forwarded to the CMOH (or designate) by phone, fax or electronic transfer within 48 hours (two business days):
  - name,
  - date of birth,
  - out-of-province health care number,
  - out-of-province address and phone number,
  - positive laboratory report, and
  - other relevant clinical/epidemiological information.

Epidemiology

Etiology

Haemolytic uremic syndrome can be classified as diarrhea-associated (D^+ HUS) or non-diarrhea-associated or atypical (D^- HUS).[1]

Verotoxigenic *E. coli* (VTEC) serotype O157:H7 is thought to cause > 90% of cases of D^+HUS in North America. Illnesses caused by other infectious organisms such as *Shigella dysenteriae* can also lead to HUS.[2] D^-HUS has been associated with various non-enteric infections, viruses, drugs, malignancies, transplantation, pregnancy, autoimmune disorders and other underlying medical conditions.[3] HUS can also occur sporadically or within families.[4] Infections caused by *Streptococcus pneumoniae* have been linked to 40% of D^-HUS cases.[3,5]

NOTE: Verotoxigenic *E. coli* (VTEC) may also be referred to as verotoxin-producing *E. coli*, enterohaemorrhagic *E. coli* (EHEC), Shiga toxin-producing *E. coli* (STEC) and verocytotoxin-producing *E. coli*.

Clinical Presentation

Haemolytic uremic syndrome (HUS) is a clinical syndrome characterized by acute renal failure, haemolytic anemia and thrombocytopenia.[1] The initial prodromal clinical presentation will vary depending on the infecting organism (refer to specific guidelines, e.g., *Escherichia coli* Verotoxigenic Infections, Shigellosis, Invasive Pneumococcal Disease).

Approximately 15% of children with *E. coli* O157:H7 diarrhea and a smaller proportion of adults develop HUS; 50% of patients will require dialysis and as high as 5% will die. Rates differ for other serotypes.[1] HUS is a microangiopathic, haemolytic anemia with the kidneys being the most vulnerable target organ. However, any tissue can be affected and become ischemic from capillary and large vessel thrombosis. Other organs that may potentially be affected include the brain (stroke), pancreas (pancreatitis) and colon (ischemic colon).[6]

HUS is the most common cause of acute renal failure in young children.[6,7,8] The illness can be life threatening and typically develops within the first week (up to three weeks) after onset of hemorrhagic (bloody) diarrhea in VTEC infections.[9] Initial symptoms of VTEC infections include severe abdominal pain and non-bloody diarrhea, which usually progresses to bloody diarrhea. Fever occurs in less than 1/3 of cases. Hemorrhagic colitis can result from severe infections.[9] Gastrointestinal symptoms may resolve before the onset of anemia and renal failure symptoms of HUS. The anemia and uremia usually presents with pallor, lethargy and irritability. Other symptoms may include hypertension, oliguria, edema and macroscopic hematuria.[7] Neurological complications such as seizure, stroke and coma can occur in 25% of HUS patients, as well as chronic renal sequelae, usually mild.[10]

Atypical HUS (D^-HUS) cases can occur following non-specific, non-diarrheal illnesses and without a seasonal tendency.[5] Individuals may have a slow, progressive course, with an insidious development of HUS. Neurological symptoms with convulsions and alterations of consciousness can be more often seen. Children will have hypertension at onset. Renal involvement will be exhibited by oliguria or anuria, high renal retention values or degradation of the creatinine clearance.[8] There may be a familial aspect to atypical HUS and has a worse long-term prognosis as compared to typical HUS.

Diagnosis

Diagnosis of HUS is based on clinical history, physical exam and laboratory manifestations as outlined in the case definition.

Treatment

Treatment is generally supportive care and may involve dialysis for individuals with renal failure.

Reservoir

This will depend on the etiologic agent. Refer to the specific guideline.

Transmission

This will depend on the etiologic agent. Refer to the specific guideline.

Incubation Period

This will depend on the etiologic agent. Refer to the specific guideline.

Period of Communicability

This will depend on the etiologic agent. Refer to the specific guideline.

Host Susceptibility

People of any age can be affected but children under five years of age and the elderly are at greatest risk of developing VTEC/STEC induced HUS.[2,6] Atypical HUS (non-diarrhea associated) may occur at all ages but it is more frequently seen in adults and prognosis is generally poorer.[8]

Incidence

General

Incidence of *E .coli* O157:H7 infections and HUS are increased in the summer and fall months. This may or may not be attributed to seasonal environmental or food exposures, or to seasonally varying levels of contamination from these or other vehicles of transmission.[11]

E. coli infections and HUS appear to be more prevalent in the Northern Hemisphere and in latitudes farther away from the equator; however, there are notable exceptions. Buenos Aires and Argentina, which are both below the equator, have a high prevalence of HUS cases.[11] This is related to their strong beef industry.[18] In 2004, the overall rate of *E. coli* O157:H7 infection for Canada was 3.36 per 100,000 persons, while Alberta's rate was more than double at 8.96 per 100,000 persons.[12] Cattle serve as a recognized reservoir for *E. coli* O157, as the organism can reside asymptomatically in the animal's intestinal tract.[13] The principle source of human infection is due to fecal contamination of food and water sources. Studies have shown a spatial association between cattle density and the incidence of human *E. coli* O157 infection.[14]

In countries that lack the resources for diagnosis of the infection, rates of *E. coli* infections are probably underestimated.[11]

In the spring of 2012, a large outbreak of severe illness caused concern in Germany with reported deaths and increased numbers of HUS cases. The pathogen associated with this outbreak is *E. coli* O104. The outbreak was unusual in that it developed very quickly and affected high numbers of adults, particularly women, instead of the normal high-risk groups which are young children and the elderly.[10]

Canada

HUS is not currently nationally notifiable. The Canadian Paediatric Surveillance Program (CPSP) conducted surveillance on incidence of HUS from April 2000 to March 2002. Based on the CPSP case definition, 140 confirmed cases of HUS were reported to December 31, 2002. Study data indicated that $HUS^{+}D$ constituted a significant public health concern in Canadian children less than five years of age. Median age was 3.7 years (0.08-15.5). From the 121 completed reports received, most children with $HUS^{+}D$ were within the one to four years age group: < 1 year (7%); 1–4 years (56%); 5–9 years (26%); 10–15

years (11%). Based on population figures from Statistics Canada at the time, the incidence of HUS^{+}D was 1.92 per 100,000 and 4.19 per 100,000 among those aged less than five years old. Thirty-four per cent of children with HUS^{+}D required dialysis during the acute phase of the illness. The mortality rate was 4%. All *Streptococcus pneumoniae* associated cases required dialysis during the course of their illness.[15]

Alberta

The incidence rate of HUS in Alberta between 2000 and 2011 ranged from 0.06 – 0.38 cases per 100,000 (average of 0.20 cases per 100,000). Eighty cases were reported during this period (average of 6.6 cases per year) affecting individuals from 0–87 years of age. The median age was three years and the majority of cases, 52/80 (65%), occurred in the ≤ five years of age group.

Refer to the Interactive Health Data Application for up-to-date surveillance information:
http://www.ahw.gov.ab.ca/IHDA_Retrieval/ihdaData.do

Public Health Management

Key Investigation

- Confirm the diagnosis.
- Obtain a history of illness including date of onset and signs and symptoms including any history of diarrheal illness in the recent past (e.g., usually within the previous two weeks).
- Determine occupation of the case. Further follow-up may be necessary depending on the causative organism. See agent-specific guidelines.
- If the case is a child, determine attendance at a child care facility (e.g., daycare, day home) or other child care site or school attended and grade. Further follow-up may be necessary depending on the causative organism. See agent-specific guidelines.
- Determine the initial possible source of infection, taking into account the incubation period, reservoir and mode of transmission of the infectious agent. Refer to specific guidelines. Assessment may include but is not limited to (depending on the suspected infectious agent):
  - taking a detailed food history, if applicable (e.g., consumption of raw or undercooked ground beef or other possibly contaminated foods),
  - inquiring about contact with animals, and
  - inquiring about food handling practices.

Management of a Case

- Early recognition of the illness is essential to the successful management. The initial clinical presentation gives a strong indication as to the underlying cause.
- Cases should be managed according to the guidelines of the causative organism (e.g., VTEC, shigellosis, invasive pneumococcal disease) unless it is unknown, in which case further investigation may be necessary. Discussion with the MOH would be appropriate.

  NOTE: VTEC should be tested in stool from patients diagnosed with post-diarrheal HUS. However, since HUS is typically diagnosed a week or more after onset of diarrhea when the organism may not be detectable by conventional methods, the absence of VTEC in stool does not preclude the diagnosis of probable VTEC-associated HUS.[9]

Management of Contacts

Contacts should be managed according to the guidelines of the causative organism for the case (e.g., VTEC, shigellosis, invasive pneumococcal disease).

Preventive Measures

Prevention of HUS is largely dependent on control of the spread of VTEC and steps include the following.

- Emphasizing the importance of good sanitation and personal hygiene including thorough hand washing, especially:
  - after using the washroom and changing diapers, and
  - before eating and preparing/handling foods.
- Encouraging hand washing after contact with animals or their environments (e.g., at farms, petting zoos).
- Ensuring that slaughterhouses maintain strict operations to minimize fecal contamination during slaughtering and processing.[2]
- Educating about safer food handling practices,[17] which include:
  - cooking meats thoroughly (especially hamburger) and to the proper internal temperature,

- avoiding raw milk, unpasteurized dairy products, and unpasteurized juices (like fresh apple cider),
- washing fruits and vegetables, especially if eaten raw (preferably, these should be peeled),
- washing and sanitizing work surfaces (e.g., counters, cutting boards) and equipment used for food preparation,
- preventing cross-contamination by avoiding contact between raw and prepared foods (using separate equipment and utensils for handling raw foods),
- following cooking and storage instructions for all foods,
- keeping foods at safe temperatures,
- checking “best before” dates, and
- using safe water.

- Early diagnosis enables early supportive treatment to be initiated and public health measures to be implemented to prevent further cases.

Appendix 1: Revision History

Revision Date	Document Section	Description of Revision
October 2021	General	• Updated Template • Etiology, Clinical Presentation, Diagnosis and Treatment sections moved to Epidemiology • Key Investigation section moved to Public Health Management (formerly called Control) • Updated web links

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