APPENDICES

APPENDIX A
EXANTHEMS—DIFFERENTIAL DIAGNOSIS

(Revised 1.10.24)

Diseases	Incubation	Prodromal Signs and Symptoms	Nature of Eruption	Other Diagnostic Features
Chickenpox (Varicella)	2-3 weeks, usually 13-17 days	0-1 day of fever, anorexia, headache. Communicable 1-2 days before and as long as 5 days after rash onset.	Rapid evolution of macules to papules, vesicles, crusts; all stages simultaneously present; lesions superficial, distribution centripetal.	Lesions on scalp and mucous membranes, predominantly on trunk. Pruritic: heals with crusty, slightly adherent scab.
Exanthem subitem (Roseola infantum, HIV-6, Human herpes virus 6)	About 10 days	3-4 days of high fever	As fever falls, pink maculopapules appear on chest and trunk; fade in 1- 3 days.	Posterior occipital lymphadenopathy. Usually under 4 years of age, commonly at about 1 year of age.
Fifth disease (Erythema infectiosum, Parvovirus B-19)	4-14 days, estimated	None; occurs as outbreaks among children.	Red, flushed cheeks; circumoral pallor; maculopapules on extremities.	"Slapped cheek" appearance. Evanescent rash with lacy appearance for 1-5 weeks.
Infectious mononucleosis (Epstein-Barr Mononucleosis)	4-6 weeks or longer	Fever, adenopathy, sore throat; communicability prolonged.	Maculopapular, pink; begins on head and neck, spreads downward; fades in 3 days. No desquamation.	Lymphadenopathy, post-auricular or occipital. Transient arthralgias may occur 2-4 weeks following rash in adults.
Mpox	3-17 days	Fever, chills, lymphadenopathy, malaise, myalgias, or headache can occur before rash but may occur after rash or not at all. Rash usually develops 1-4 days later.	Painful or itchy, firm or rubbery, well-circumscribed, deep-seated, and often develop umbilication lesions (resembles a dot on the top of the lesion). Initially looks like pimples or blisters may be located on hands, feet, chest, face, or mouth or near the genitals, including penis, testicles, labia, and vagina, and anus.	Fever, chills, swollen lymph nodes, exhaustion, muscle aches and backache, headache, respiratory symptoms (e.g., sore throat, nasal congestion, or cough)
Rubella (German Measles)	14-21 days, usually 18 days	Little or no prodrome. Communicable 1 week before rash and 4 days after.	Maculopapular rash resembling measles or scarlet fever, rarely papulovesicular.	Splenomegaly, adenopathy, and hepatomegaly.
Rubeola (Measles)	8-13 days, usually 10 days	3-4 days of fever, coryza, conjunctivitis, and cough. Communicable from about 4 days prior to rash to 4 days after.	Maculopapular, reddish-brown; begins on head and neck, spreads downward. In 5-6 days rash turns brownish, desquamating.	Koplik's spots on buccal mucosa. General lymphadenopathy, occasional splenomegaly; encephalitis.
Scarlet fever (Scarlatina)	1-3 days	1-2 days of malaise, sore throat, fever, vomiting. Usually non- communicable 24-48 hours after antibiotics started. If untreated, can be communicable for 2-3 weeks.	Generalized, punctuate, red; prominent on chest, neck, axilla, groin, skin folds; circumoral pallor; fine desquamation involves hands and feet. Rash is sandpaper-like to touch and blanches on pressure.	Strawberry tongue, exudative tonsillitis; general cervical adenopathy.
Smallpox (Variola)	7-19 days, usually 10-14 days	Occurring 1-4 days before rash onset, fever and at least 1 of the following: prostration, headache, backache, chills, vomiting, or severe abdominal pain.	Greatest concentration of lesions on face and distal extremities. Lesions are deep seated, firm/hard, round well-circumscribed vesicles or pustules at the same stage of development on same part of body.	First lesions on the oral mucosa/palate, face or forearms. Lesions occur on palms and soles. Patient appears toxic or moribund.

Appendix B

Guidelines for Confirmation of Foodborne-Disease Outbreaks

A foodborne-disease outbreak (FBDO) is defined as an incident in which two or more persons experience a similar illness resulting from the ingestion of a common food.* The following table provides information about incubation periods, clinical syndromes, and criteria for confirming the etiology once an FBDO has been identified. The information on incubation periods and clinical syndromes is provided as a guideline and should not be included in the confirmation criteria. These guidelines might not include all etiologic agents and diagnostic tests.

FBDOs should be reported to the Foodborne and Diarrheal Diseases Branch at CDC on Form 52.13, Investigation of a Foodborne Outbreak, which was updated in October 1999. Provision of other documents describing the outbreak investigation also is encouraged. For information regarding collection of laboratory specimens and for additional information on viral agents, refer to other CDC publications (i.e., "Recommendations for Collection of Laboratory Specimens Associated with Outbreaks of Gastroenteritis," *MMWR* 1990:39[No. RR-14] and "Viral Agents of Gastroenteritis: Public Health Importance and Outbreak Management," *MMWR* 1990;39[No. RR-5]).

*Before 1992, three exceptions existed to this definition; only one case of botulism, marine-toxin intoxication, or chemical intoxication was required to constitute an FBDO if the etiology was confirmed. The definition was changed in 1992 to require two or more cases to constitute an outbreak.

Table B. Guidelines for confirmation of foodborne-disease outbreaks

Etiologic agent	Incubation period	Clinical syndrome	Confirmation
Bacterial			
1. *Bacillus cereus*			
a. Vomiting toxin	1–6 hrs	Vomiting; some patients with diarrhea; fever uncommon	Isolation of organism from stool of two or more ill persons and not from stool of control patients OR Isolation of 10^5 organisms/g from epidemiologically implicated food, provided specimen is properly handled
b. Diarrheal toxin	6–24 hrs	Diarrhea, abdominal cramps, and vomiting in some patients; fever uncommon	Isolation of organism from stool of two or more ill persons and not from stool of control patients OR Isolation of 10^5 organisms/g from epidemiologically implicated food, provided specimen is properly handled
2. *Brucella*	Several days to several mos; usually >30 days	Weakness, fever, headache, sweats, chills, arthralgia, weight loss, splenomegaly	Two or more ill persons and isolation of organism in culture of blood or bone marrow; greater than fourfold increase in standard agglutination titer (SAT) over several wks, or single SAT 1:160 in person who has compatible clinical symptoms and history of exposure
3. *Campylobacter jejuni/coli*	2–10 days; usually 2–5 days	Diarrhea (often bloody), abdominal pain, fever	Isolation of organism from clinical specimens from two or more ill persons OR Isolation of organism from epidemiologically implicated food

Table B. (*Continued*) Guidelines for confirmation of foodborne-disease outbreaks

Etiologic agent	Incubation period	Clinical syndrome	Confirmation
4. *Clostridium botulinum*	2 hrs–8 days; usually 12–48 hrs	Illness of variable severity; common symptoms are diplopia, blurred vision, and bulbar weakness; paralysis, which is usually descending and bilateral, might progress rapidly	Detection of botulinal toxin in serum, stool, gastric contents, or implicated food OR Isolation or organism from stool or intestine
5. *Clostridium perfringens*	6–24 hrs	Diarrhea, abdominal cramps; vomiting and fever uncommon	Isolation of 10^5 organisms/g from stool of two or more ill persons, provided specimen is properly handled. OR Demonstration of enterotoxin in the stool of two or more ill persons OR Isolation of 10^5 organisms/g from epidemiologically implicated food, provided specimen is properly handled
6. *Escherichia coli*			
a. Enterohemorrhagic (*E. coli* O157:H7 and others)	1–10 days; usually 3–4 days	Diarrhea (often bloody), abdominal cramps (often severe), little or no fever	Isolation of *E. coli* O157:H7 or other Shiga-like toxin-producing *E. coli* from clinical specimen from two or more ill persons OR Isolation of *E. coli* O157:H7 or other Shiga-like toxin-producing *E. coli* from epidemiologically implicated food
b. Enterotoxigenic (ETEC)	6–48 hrs	Diarrhea, abdominal cramps, nausea; vomiting and fever less common	Isolation of organism of same serotype, demonstrated to produce heat-stable (ST) and/or heat-labile (LT) enterotoxin, from stool of two or more ill persons
c. Enteropathogenic (EPEC)	Variable	Diarrhea, fever, abdominal cramps	Isolation of organism of same enteropathogenic serotype from stool of two or more ill persons

Table B. (*Continued*) Guidelines for confirmation of foodborne-disease outbreaks

Etiologic agent	Incubation period	Clinical syndrome	Confirmation
d. Enteroinvasive (EIEC)	Variable	Diarrhea (might be bloody), fever, abdominal cramps	Isolation of same enteroinvasive serotype from stool of two or more ill persons
7. *Listeria monocytogenes*			
a. Invasive disease	2–6 wks	Meningitis, neonatal sepsis, fever	Isolation of organism from normally sterile site
b. Diarrheal disease	Unknown	Diarrhea, abdominal cramps, fever	Isolation of organism of same serotype from stool of two or more ill persons exposed to food that is epidemiologically implicated or from which organism of same serotype has been isolated
8. Nontyphoidal *Salmonella*	6 hrs–10 days; usually 6–48 hrs	Diarrhea, often with fever and abdominal cramps	Isolation of organism of same serotype from clinical specimens from two or more ill persons OR Isolation of organism from epidemiologically implicated food
9. *Salmonella* Typhi	3–60 days; usually 7–14 days	Fever, anorexia, malaise, headache, and myalgia; sometimes diarrhea or constipation	Isolation of organism from clinical specimens from two or more ill persons OR Isolation of organism from epidemiologically implicated food
10. *Shigella* spp.	12 hrs–6 days; usually 2–4 days	Diarrhea (often bloody), often accompanied by fever and abdominal cramps	Isolation of organism of same serotype from clinical specimens from two or more ill persons OR Isolation of organism from epidemiologically implicated food

Table B. (*Continued*) Guidelines for confirmation of foodborne-disease outbreaks

Etiologic agent	Incubation period	Clinical syndrome	Confirmation
11. *Staphylococcus aureus*	30 min–8 hrs; usually 2–4 hrs	Vomiting, diarrhea	Isolation of organism of same phage type from stool or vomitus of two or more ill persons OR Detection of enterotoxin in epidemiologically implicated food OR Isolation of 10^5 organisms/g from epidemiologically implicated food, provided specimen is properly handled
12. *Streptococcus,* group A	1–4 days	Fever, pharyngitis, scarlet fever, upper respiratory infection	Isolation of organism of same M- or T-type from throats of two or more ill persons OR Isolation of organism of same M- or T-type from epidemiologically implicated food
13. *Vibrio cholerae*			
a. O1 or O139	1–5 days	Watery diarrhea, often accompanied by vomiting	Isolation of toxigenic organism from stool or vomitus of two or more ill persons OR Significant rise in vibriocidal, bacterial-agglutinating, or antitoxin antibodies in acute- and early convalescent-phase sera among persons not recently immunized OR Isolation of toxigenic organism from epidemiologically implicated food
b. non-O1 and non-O139	1–5 days	Watery diarrhea	Isolation of organism of same serotype from stool of two or more ill persons

Table B. (*Continued*) Guidelines for confirmation of foodborne-disease outbreaks

Etiologic agent	Incubation period	Clinical syndrome	Confirmation
14. *Vibrio parahaemolyticus*	4–30 hrs	Diarrhea	Isolation of Kanagawa-positive organism from stool of two or more ill persons OR Isolation of 10^5 Kanagawa-positive organisms/g from epidemiologically implicated food, provided specimen is properly handled
15. *Yersinia enterocolitica*	1–10 days; usually 4–6 days	Diarrhea, abdominal pain (often severe)	Isolation of organism from clinical specimen from two or more ill persons OR Isolation of pathogenic strain of organism from epidemiologically implicated food
Chemical			
1. Marine toxins			
a. Ciguatoxin	1–48 hrs; usually 2–8 hrs	Usually gastrointestinal symptoms followed by neurologic symptoms (including paresthesia of lips, tongue, throat, or extremities) and reversal of hot and cold sensation	Demonstration of ciguatoxin in epidemiologically implicated fish OR Clinical syndrome among persons who have eaten a type of fish previously associated with ciguatera fish poisoning (e.g., snapper, grouper, or barracuda)
b. Scombroid toxin (histamine)	1 min–3 hrs; usually <1 hr	Flushing, dizziness, burning of mouth and throat, headache, gastrointestinal symptoms, urticaria, and generalized pruritis	Demonstration of histamine in epidemiologically implicated fish OR Clinical syndrome among persons who have eaten a type of fish previously associated with histamine fish poisoning (e.g., mahi-mahi or fish of order Scomboidei)

Table B. (*Continued*) Guidelines for confirmation of foodborne-disease outbreaks

Etiologic agent	Incubation period	Clinical syndrome	Confirmation
c. Paralytic or neurotoxic shellfish	30 min–3 hrs	Paresthesia of lips, mouth or face, and extremities; intestinal symptoms or weakness, including respiratory difficulty	Detection of toxin in epidemiologically implicated food OR Detection of large numbers of shellfish-poisoning–associated species of dinoflagellates in water from which epidemiologically implicated mollusks are gathered
d. Puffer fish, tetrodotoxin	10 min–3 hrs; usually 10–45 min	Paresthesia of lips, tongue, face, or extremities, often following numbness; loss of proprioception or floating sensations	Demonstration of tetrodotoxin in epidemiologically implicated fish OR Clinical syndrome among persons who have eaten puffer fish
2. Heavy metals • Antimony • Cadmium • Copper • Iron • Tin • Zinc	5 min–8 hrs; usually <1 hr	Vomiting, often metallic taste	Demonstration of high concentration of metal in epidemiologically implicated food
3. Monosodium glutamate (MSG)	3 min–2 hrs; usually <1 hr	Burning sensation in chest, neck, abdomen, or extremities; sensation of lightness and pressure over face or heavy feeling in chest	Clinical syndrome among persons who have eaten food containing MSG (e.g., usually 1.5 g MSG)
4. Mushroom toxins			
a. Shorter-acting toxins	2 hrs	Usually vomiting and diarrhea, other symptoms differ with toxin	Clinical syndrome among persons who have eaten mushroom identified as toxic type OR Demonstration of toxin in epidemiologically implicated mushroom or food containing mushroom
• Muscimol		• Confusion, visual disturbance	
• Muscarine		• Salivation, diaphoresis	
• Psilocybin		• Hallucinations	
• *Coprinus artrementaris*		• Disulfiram-like reaction	
• Ibotenic acid		• Confusion, visual disturbance	

Table B. (*Continued*) Guidelines for confirmation of foodborne-disease outbreaks

Etiologic agent	Incubation period	Clinical syndrome	Confirmation
b. Longer-acting toxins (e.g., *Amanita* spp.)	6–24 hrs	Diarrhea and abdominal cramps for 24 hrs followed by hepatic and renal failure	Clinical syndrome among persons who have eaten mushroom identified as toxic type OR Demonstration of toxin in epidemiologically implicated mushroom or food containing mushrooms
Parasitic			
1. *Cryptosporidium parvum*	2–28 days; median: 7 days	Diarrhea, nausea, vomiting; fever	Demonstration of organism or antigen in stool or in small-bowel biopsy of two or more ill persons OR Demonstration of toxin in epidemiologically implicated food
2. *Cyclospora cayetanensus*	1–11 days; median: 7 days	Fatigue, protracted diarrhea, often relapsing	Demonstration of organism in stool of two or more ill persons
3. *Giardia lamblia*	3–25 days; median: 7 days	Diarrhea, gas, cramps, nausea, fatigue	Two or more ill persons and detection of antigen in stool or demonstration of organism in stool, duodenal contents, or small-bowel biopsy specimen
4. *Trichinella* spp.	1–2 days for intestinal phase; 2–4 wks for systemic phase	Fever, myalgia, periorbital edema, high eosinophil count	Two or more ill persons and positive serologic test or demonstration of larvae in muscle biopsy OR Demonstration of larvae in epidemiologically implicated meat

Table B. (*Continued*) Guidelines for confirmation of foodborne-disease outbreaks

Etiologic agent	Incubation period	Clinical syndrome	Confirmation
Viral			
1. Hepatitis A	15–50 days; median: 28 days	Jaundice, dark urine, fatigue, anorexia, nausea	Detection of immunoglobulin M anti-hepatitis A virus in serum from two or more persons who consumed epidemiologically implicated food
2. Norwalk family of viruses, small round-structured viruses (SRSV)	15–77 hrs; usually 24–48 hrs	Vomiting, cramps, diarrhea, headache	More than fourfold rise in antibody titer to Norwalk virus or Norwalk-like virus in acute and convalescent sera in most serum pairs OR Visualization of small, round-structured viruses that react with patient's convalescent sera but not acute sera — by immune-electron microsopy (assays based on molecular diagnostics [e.g., polymerase-chain reaction, probes, or assays for antigen and antibodies from expressed antigen] are available in reference laboratories)
3. Astrovirus, calicivirus, others	15–77 hrs; usually 24–48 hrs	Vomiting, cramps, diarrhea, headache	Visualization of small, round-structured viruses that react with patient's convalescent sera but not acute sera — by immune-electron microsopy (assays based on molecular diagnostics [e.g., polymerase-chain reaction, probes, or assays for antigen and antibodies from expressed antigen] are available in reference laboratories)

MMWR

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APPENDIX C
VIRAL HEPATITIS - DIFFERENTIAL DIAGNOSIS

	HEPATITIS A	HEPATITIS B	HEPATITIS C
Agent	HAV (hepatitis A virus), an RNA virus related to enteroviruses	HBV (hepatitis B virus), a double-stranded DNA virus.	HCV (hepatitis C virus), a single-stranded RNA virus.
Transmission	Fecal-oral: Person to person, contaminated food.	By parenteral inoculation or mucosal membrane exposure to human blood or blood products. Sexual contact, contaminated IV needles, razors, tattoo/body piercing and other sharp instruments. Perinatal transmission.	Parenteral or permucosal exposure to contaminated blood or blood products. Transmission by sexual and perinatal exposure is possible but uncommon.
Incubation	15-50 days (average 28-30 days).	45-180 days (average 60-90 days).	15-180 days (average 40 days).
Source	Feces from infected human, rarely blood.	Blood or blood products; semen.	Blood or blood products.
Communicability	Two weeks prior to onset of jaundice. Not infectious 1 week after onset of jaundice.	Several weeks before onset of jaundice for as long as HBsAg present.	From one or more weeks prior to onset; may persist indefinitely. Carrier state is common. Viremia appears to be relatively low.
Diagnosis	An acute illness with 1) discrete onset of symptoms **and** 2) jaundice or elevated serum aminotransferase levels **AND** based on positive IgM specific hepatitis A virus antibody test (anti-HAV IgM). Total hepatitis A virus antibody (Total anti-HAV) is not a confirmatory test for acute HAV. A case meets the clinical definition and occurs in a person who has an epidemiologic link with a person who has laboratory-confirmed hepatitis A (i.e., household or sexual contact with an infected person during the 15-50 days before the onset of symptoms).	Acute case: 1) discrete onset of symptoms, and 2) jaundice or elevated aminotransferase levels, and 3) appropriate lab tests for confirmation: HbsAg positive and/or anti-HBc IgM positive (if done), and 4) anti-HAV IgM negative (if done).	Acute case: 1) discrete onset of symptoms and 2) jaundice or ALT>7 times the upper limit of normal; and 3) IgM anti-HAV negative (if done), and 4) IgM anti-HBc negative (if done) or HbsAg negative and 5) anti-HCV positive by EIA, verified by an additional more specific assay (e.g. RIBA for anti-HCV or RT-PCR for HCV RNA) or by an average EIA signal to cutoff ratio of $\geq$3.8.
Treatment	None specific; supportive. No carrier state.	Antiviral medications help about one-third; supportive Chronic HBV disease occurs in 5-10% of acute cases with one third of these showing active liver disease with poor prognosis.	Treatment with interferon alone or in combination with ribravirin may be effective in 10-20% of cases with chronic disease.
Prophylaxis/ Vaccine	Immune globulin (IG) - see B-71. Hepatitis A vaccine.	HBIG: acute exposure (see B-71). Hepatitis B vaccine; for long-term exposure (see B-71).	IG of no known benefit; no vaccine available.
Laboratory Test	Anti-HAV IgM.	Various serological tests available (see table in the hepatitis B chapter). Transaminase and bilirubin levels are used to monitor course of disease and liver function.	Liver function tests, anti-HAV IgM, HBsAg,anti-HBc IgM, second or third-generation EIA for HCV antibody(anti-HCV),RIBA, RT-PCR.
Signs/Symptoms	Abrupt onset with fever, malaise, anorexia, abdominal discomfort, jaundice, nausea & vomiting, and hepatomegaly. Chronic liver disease with cirrhosis not documented. Fulminating liver disease with coma rare. With acute hepatic failure, mortality rate is 65-75%. Severity increases with age. Often asymptomatic in infants and small children.	Insidious onset with anorexia, malaise, abdominal discomfort, jaundice and arthralgias. For carriers, can progress to chronic liver disease and cirrhosis. With acute hepatic failure, mortality rate is 65-75%. Severity increases with age. Asymptomatic in 70% of cases. 15-25% of those with chronic infection will develop liver cancer.	Often asymptomatic, mild disease. 10%-20% have vague symptoms such as anorexia, malaise or abdominal pain, 20-30% have jaundice, 85% become chronic carriers, 70% develop chronic liver disease, 15% develop cirrhosis after 20 to 30 years, 5% die from liver cancer or cirrhosis. Fulminant hepatic failure following infection is rare.
Synonyms	Infectious hepatitis (obsolete).	Serum hepatitis, Australian antigen (both obsolete).	Hepatitis non-A, non-B (obsolete).