CLOSTRIDIUM DIFFICILE

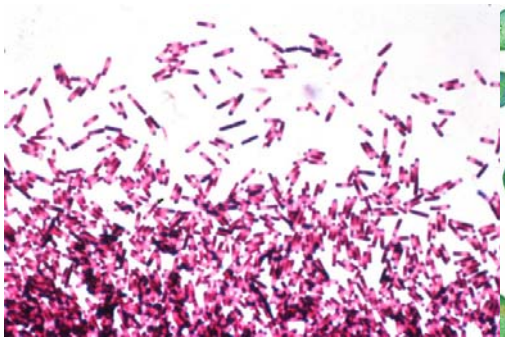
PATHOGEN SAFETY DATA SHEET - INFECTIOUS SUBSTANCES

INFECTIOUS AGENT

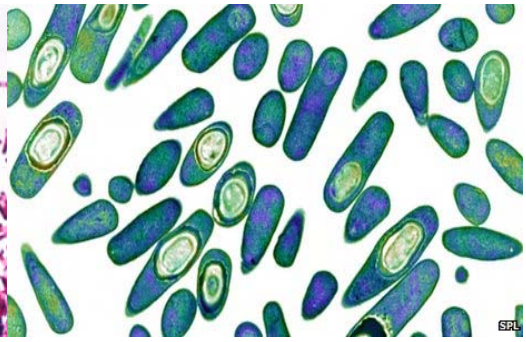
NAME: *Clostridium difficile*

SYNONYM OR CROSS REFERENCE: *Clostridium difficile is also called C. difficile, C. diff, and* CDI (*Clostridium difficile* infection), CDAD (*Clostridium difficile*-associated disease), Pseudomembranous colitis, *C. difficile* colitis.

CHARACTERISTICS: *Clostridium difficile*, of the *Clostridiaceae* family, is Gram positive, motile, anaerobic, and spore-forming (forms subterminal spores). Vegetative cells are rod shaped, pleomorphic, and occur in pairs or short chains. It is catalase and superoxide dismutase negative and produces 2 types of toxins: enterotoxin A and cytotoxin B, which disrupts cytoskeleton signal transductions in the host.



Clostridium difficile, gram-stained[1)]



Clostridium difficile cells and spores[2)]

HAZARD IDENTIFICATION

PATHOGENICITY: *C. difficile* is the main cause of nosocomial antibiotic-associated diarrhea. Antibiotics or any other procedures that disrupt the normal intestinal microbiota can lead to the overgrowth and production of toxin by *C. difficile*, which leads to clinical manifestations of infection. The diarrhea may range from a few days of intestinal fluid loss to life-threatening pseudomembranous colitis (PMC). In diarrhea without PMC, feces have a foul odor and are not bloody. Abdominal pain with or without pyrexia may also be present along with diarrhea. PMC is associated with intense inflammation of the colon and formation of pseudomembranes on the intestinal mucosal surface. Patients with PMC also have more systemic side effects. Rare extracolonic manifestations of *C. difficile* infection include bacteremia, intra-abdominal abscess, osteomyelitis, visceral abscess, empyema, toxic megacolon, colonic perforation, and reactive arthritis. The production of exotoxins A and B facilitates tissue damage, which results in cell necrosis and ulceration, diarrhea and fluid secretion, and colitis. The strain with ribotype 027, also known as North America Pulsotype (NAP) 1, is one of the most pathogenic types of *C. difficile*, and the severity of this strain is based on its unusually high levels of toxin A and B production, its production of a third toxin known as the binary toxin, and its resistance to fluoroquinolone antibiotics. Another new hypervirulent *C. difficile* strain 078 (NAP7/8) has been associated with severe diarrhea and high mortality rates have been reported from e.g., The Netherlands and Canada.

EPIDEMIOLOGY: *C. difficile* is of worldwide prevalence as 2-5% of the normal healthy adults carry the bacteria as a part of normal gut microflora, and older people tend to have a higher percentage (10-20%) of colonization. The main risk factors for *C. difficile* infections include frail elderly, peripartum women and children, and antibiotic therapy. The number of severe *C. difficile* outbreaks associated with high mortality has increased in North America and Europe since 2000, and these outbreaks are associated with strain 027. The incidence of strain 078 has increased from 3% to 13% from February 2005 to February 2008.

HOST RANGE: Humans and other animals.

INFECTIOUS DOSE: Not known.

MODE OF TRANSMISSION: Transmission mainly occurs through the fecal-oral route, via contaminated foods, fomites, or hands. *C. difficile* overgrowth and toxin production can occur in immunocompromised patients from their natural flora. Nosocomial transmission has also been reported, where infections were transmitted via hospital staff and contaminated equipment.

INCUBATION PERIOD: 5-10 days with a range of 1 day to weeks following antibiotic treatment for antibiotic associated diarrhea (AAD).

COMMUNICABILITY: Low risk of transmission from person-to-person, although nosocomial transmission from contaminated hands, instruments such as endoscopes, and the environment have been reported. Asymptomatic patients can also act as a reservoir for the transmission of this pathogen within the hospital.

DISSEMINATION

RESERVOIR: Soil, feces of domestic animals and humans, sewage, human intestinal tract, and retail meat. **ZOONOSIS:** No evidence of direct transmission from animals to humans, but indirect transmission can occur via contaminated food.

VECTORS: None

STABILITY AND VIABILITY

DRUG SUSCEPTIBILITY: Susceptible to metronidazole and oral vancomycin. *C. difficile* also demonstrates sensitivity to penicillins and cephalosporins *in vitro*, but these drugs are not used for treatment because they can be destroyed by β-lactamases/cephalosporinases produced by other intestinal bacteria and are, thus, ineffective for treatment in vivo.

DRUG RESISTANCE: Some rare strains resistant to metronidazole have been isolated. Fluoroquinolone-resistant hypervirulent strain 027 has also been isolated from North America and Europe.

SUSCEPTIBILITY TO DISINFECTANTS: Spores are generally resistant to disinfection. *Clostridium* spores are resistant to ethyl and propyl alcohols. High level disinfectants such as 2% glutaraldehyde can kill spores within 20 minutes. 8% formaldehyde and 20 ppm sodium hypochlorite are also effective against bacterial spores.

PHYSICAL INACTIVATION: Spores of the genus *Clostridium* are generally heat resistant and can withstand temperature of 116°C for 3 hours, whereas their vegetative cells can be rapidly killed by temperatures of only 55-65°C. Most spores can be inactivated by moist heat at 121°C for 15-30 minutes.

SURVIVAL OUTSIDE HOST: *C. difficile* is able to survive in soil, meat, and vegetables.

FIRST AID / MEDICAL

SURVEILLANCE: Monitor for symptoms. Detection of toxins in stool specimens is the Gold Standard test for diagnosis of *C. difficile* infection. Detection of toxins is done using cell culture assays, or Enzyme Immunoassay (EIA). Diagnosis can also be done by culturing the bacteria on appropriate media such as egg yolk agar-based media or blood agar media. Two different approaches are commonly used for typing of *C. difficile* strains and include polymerase chain reaction (PCR)-ribotyping and pulse field gel electrophoresis (PFGE).

Note: All diagnostic methods are not necessarily available in all countries.

FIRST AID/TREATMENT: Treatment should be supportive with rebalancing of fluid levels and electrolytes. Antibiotic treatment should be discontinued for antibiotic associated diarrhea (AAD) infection. For patients who do not respond to drug withdrawal or are present with systemic illness, oral metronidazole is used for treatment. Oral vancomycin has been shown to be more effective than metronidazole in treating recurrent infections.

IMMUNIZATION: None

PROPHYLAXIS: Antibacterial prophylaxis is not recommended for *C. difficile* since antibiotics can have an adverse effect on the normal gut flora.

LABORATORY HAZARDS

LABORATORY-ACQUIRED INFECTIONS: 1 reported case of a laboratory-acquired infection from *C. difficile.*

SOURCES/SPECIMENS: Human fecal and excretion samples, contaminated food products, and bowel luminal contents or tissue.

PRIMARY HAZARDS: Accidental ingestion of the pathogen or its toxins.

SPECIAL HAZARDS: None

EXPOSURE CONTROLS / PERSONAL PROTECTION

RISK GROUP CLASSIFICATION: Risk Group 2.

CONTAINMENT REQUIREMENTS: Containment level 2 facilities, equipment, and operational practices are recommended for work involving infectious or potentially infectious materials, animals, or cultures.

PROTECTIVE CLOTHING: Laboratory coat. Gloves when direct contact with infectious materials is unavoidable. Eye protection must be used where there is a known or potential risk of exposure to splashes.

OTHER PRECAUTIONS: All procedures that may produce aerosols, or involve high concentrations or large volumes should be conducted in a biological safety cabinet (BSC). The use of needles, syringes, and other sharp objects should be strictly limited. Additional precautions should be considered with work involving animals or large scale activities.

HANDLING AND STORAGE

SPILLS: Allow aerosols to settle, wearing protective clothing, gently cover spill with paper towels and apply an appropriate disinfectant, starting at perimeter and working towards the center. Allow sufficient contact time before clean up.

DISPOSAL: Decontaminate all wastes that contain or have come in contact with the infectious organism by autoclave, chemical disinfection, gamma irradiation, or incineration before disposing.

STORAGE: The infectious agent should be stored in leak-proof containers that are appropriately labeled.

REFERENCE

Pathogen Safety Data Sheet (PSDS) for *Clostridium difficile* has been modified from the ones produced by the Public Health Agency of Canada as educational and informational resources for laboratory personnel working with infectious substances.

1) Picture from Wikipedia
2) Picture from "Welsh hospital infection rates revealed", by Owain Clarke BBC Wales health correspondent, last updated 11 July 2013.