For emergency medicine and trauma professionals

TRAUMA rounds

SUMMER 2017

In This Issue

Clostridium Difficile Infection: An Overview for Health Care Providers

by Paul Waltz, MD, and Brian Zuckerbraun, MD, FACS

Clostridium difficile (C. difficile) is responsible for nearly 500,000 infections annually and resulted in approximately 29,000 deaths in 2011. A review of the National Hospital Discharge Surveys reveals an increasing incidence, nearly doubling from 4.5 per 1,000 discharges in 2001 to 8.2 per 1,000 discharges in 2010. Clostridium difficile infection (CDI) is a leading cause of hospital-acquired infection (HAI), with an estimated economic burden exceeding $1.5 billion in the United States in 2009. Rates of outpatient diagnoses of CDI are also increasing.

Pathogenesis

C. difficile is an anaerobic, spore-forming, gram-positive organism that is transmitted via the fecal-oral route. These environmentally resistant spores are ingested and activated by bile acids in the small intestine. Once activated, the bacterium adheres to colonic mucosa. Virulence is mediated by the production of toxins A and B. These toxins result in a profound inflammatory response, alterations in cellular tight junctions, and apoptosis leading to the clinical symptoms of diarrhea.

The underlying host colonic microbiome plays an important role in the pathogenesis of CDI. The association between antibiotic administration and subsequent development of CDI has long been recognized, particularly with clindamycin, cephalosporins, and fluoroquinolones. Alterations in host microbiome from antimicrobial agents may set the stage for C. difficile colonization. This may be more complex than merely providing a "space" for the bacteria to flourish. Studies evaluating fecal microbiota before and after successful fecal microbiota therapy have shown a return to a balance of Bacteroidetes and Firmicutes species with a concomitant decrease in Enterobacteriaceae and Proteobacteria. Altered colonic flora and the interrelated metabolic products of these bacteria may play a role in pathogenesis. For example, some secondary bile acids have been shown to inhibit growth of C. difficile and may protect colonocytes from toxin-mediated damage.

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Clostridium Difficile Infection *(Continued from Page 1)*

Disease Severity

CDI encompasses a spectrum of disease severity. It is important to be precise in defining the manifestations of CDI so as to properly risk-stratify patients, provide the appropriate level of treatment, and ensure similar groups are compared when evaluating new therapies and outcomes. The guidelines published by the American College of Gastroenterology separate CDI into mild, moderate, severe, severe-complicated, or recurrent manifestations. Mild disease is CDI with diarrhea being the only symptom. Moderate disease is CDI with diarrhea and additional signs and symptoms that do not meet the following criteria for severe disease. Severe disease is defined as CDI presenting with hypoalbuminemia (<3g/dL) with either a white blood cell count (WBC) ≥15,000 cells/mm^3 or abdominal tenderness. Severe-complicated disease is defined as admission to the intensive care unit attributed to CDI, hypotension (with or without vasopressors), fever ≥38.5°C, ileus or significant abdominal distention, alterations in mental status, WBC ≥35,000 cells/mm^3, serum lactate >2.2 mmol/l, and signs of end-organ dysfunction. Finally, recurrent disease is defined as a recurrence of CDI within eight weeks of completing therapy.

The treatment of all degrees of CDI should follow the basic principles of appropriate fluid resuscitation, correction of electrolyte abnormalities, cessation of inciting antibiotics, avoidance of antimotility agents (including narcotics), and support of organ dysfunction as indicated.

Antibiotics

Current recommendations support the use of metronidazole 500mg three times daily for mild or moderate CDI and vancomycin orally at 125mg four times daily for severe CDI, both for a duration of 10 to 14 days. Severe complicated disease is often managed by an increased dosing of vancomycin 500mg four times daily along with rectal instillation of vancomycin via enema. Rectal vancomycin should also be considered when there is an ileus or the gastrointestinal tract is in discontinuity, thus preventing oral administration of vancomycin from reaching the colon (e.g., diverting ileostomy, Hartmann's pouch).

Newer antibiotics try to capitalize on characteristics that have made vancomycin an effective anti-CDI agent. This includes high intracolonic drug levels for C. difficile with minimal systemic absorption and toxicity toward other gastrointestinal flora. Fidaxomicin is a macrocyclic antibiotic that received FDA approval for CDI in 2011. Fidaxomicin as first-line treatment for CDI has been limited due to cost as compared to current treatments. Clinical cure for CDI is no different between vancomycin and fidaxomicin. However, for both severe and non-severe CDI, there appears to be a significantly lower recurrence rate associated with fidaxomicin compared to vancomycin, but no difference in sustained cure (defined as clinical cure in the absence of any recurrence during the entire study follow-up period) for severe CDI. This favorable difference in recurrence rate may offset the higher drug cost. Recent modeling has shown that fidaxomicin may be as cost effective as vancomycin in severe disease.

Fecal Microbiota Therapy

Fecal microbiota therapy (FMT) aims at restoring the colonic biodiversity. While originally described over a half-century ago by Dr. Ben Eiseman, chief of surgery at Denver General Hospital, and his colleagues, FMT has received considerable attention over the past several years as an effective treatment modality in recurrent CDI. In 2013, a randomized trial comparing standard vancomycin regimen; vancomycin and bowel lavage; or vancomycin, bowel lavage, and nasoduodenal tube infusion of donor feces, showed superior rates of resolution of recurrent CDI in the FMT group (81% resolution with initial dose of donor feces versus 31% resolution receiving vancomycin alone). A recent randomized trial comparing colonoscopic administration of FMT versus standard vancomycin regimen echoed these findings with a success rate of 90% with FMT versus 26% without FMT for recurrent CDI. A meta-analysis revealed similar high success rates with FMT of 84-93%, without an apparent difference between FMT instillation via the upper or lower gastrointestinal tract.

It again must be stressed that this experience applies primarily to the treatment of recurrent CDI. Currently, the American College of Gastroenterology recommends the consideration of FMT as an alternative treatment for recurrent CDI. The experience of FMT in the acute setting for the management of severe disease is still evolving. A small study investigated early (within one week of diagnosis of CDI) FMT use for the treatment of CDI associated with the hypervirulent ribotype 027 in geriatric patients compared to later FMT use. There was a significant difference in mortality at one month: 18.75% in the early FMT group versus 64.4% in the late group. However, severity of CDI was not clearly presented.

Novel Medical Strategies

A complementary strategy in reconstituting normal colonic microbiota involves the administration of C. difficile spores of strains that are non-toxigenic. These spores are intended to outcompete toxigenic C. difficile in the supposed ecologic niche afforded through altered microbiota. Immunologic and targeted therapy toward the C. difficile virulence factors is an attractive therapeutic modality that could potentially limit the need for antibiotics in the treatment of CDI. This includes monoclonal antibodies targeted against toxins A and B and vaccine-based strategies.

Surgical Therapy

Despite a myriad of therapeutic approaches detailed above, CDI may ultimately progress to surgical management. Absolute indications for surgical intervention include perforation and abdominal compartment syndrome, although these are not typical. The most usual indication for operative management is the development of sepsis or end-organ failure with CDI. The experienced surgical team can improve survival for such patients by making the timely decision to offer operative therapy. Traditional surgical approach for CDI is a laparotomy with total abdominal colectomy and end ileostomy. This procedure carries

a high morbidity and mortality, partly related to the comorbidities of the patient population. In a retrospective series of patients managed surgically for fulminant CDI, in-hospital mortality was found to be 41% after intervention, with a mean survival time after CDI of 18.1 months. Most patients were managed with colectomy and end ileostomy. Additionally, only 14% of patients had gastrointestinal continuity restored after resolution of illness.

The surgical team at UPMC has described a minimally invasive approach of loop ileostomy and colonic lavage in an attempt to foster earlier surgical involvement and minimize associated operative morbidity and mortality. At the time of loop ileostomy, the efferent limb of the ileostomy is cannulated with a catheter and infused with a solution of 8L of warmed polyethylene glycol 3350 and electrolytes. Following this, the loop ileostomy is used for antegrade vancomycin flushes. While retrospective, this resulted in decreased mortality from 50% in historic matched controls to 19% with loop ileostomy. Furthermore, 39 of 42 patients treated with loop ileostomy were able to maintain their colons. The benefit of this approach has recently been validated in a multicenter retrospective review of loop ileostomy and lavage versus colectomy.

Summary

C. difficile remains a disease of high prevalence, cost, recurrence, and associated mortality. Treatment remains multimodal aimed at prevention, resuscitation, and appropriate use of antimicrobial agents. The potential microbial, immunologic, and surgical therapies described here may offer new options to treating the patient with severe CDI.

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Left to right: Cheryl Six, DO; Gina Howell, MD; Alain Corcos, MD; Garth Elias, MD; Jenny Ziembicki, MD

Drowning and Near Drowning: Just When You Thought it Was Safe to Go in the Water

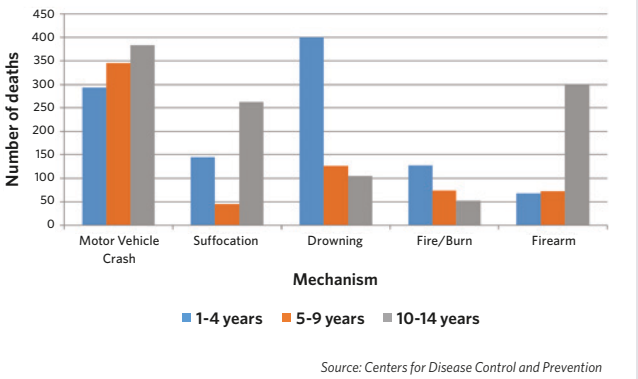
by Ward M. Richardson, MD

"No more pencils, no more books, no more teachers' dirty looks!" For millions of children, summertime means warm weather, summer camps, pools, and beach vacations. However, for both pediatric and adult trauma surgeons alike, it also means more business. Trauma is the leading cause of death and disability among children older than one year of age. Summer months see a rise in the incidence of trauma among kids, due in large part to an increase in activities with less supervision by adults and an increase in overall risk of activities. Warmer weather brings more exposure to bodies of water and, resultantly, an increase in drownings, with two-thirds of drowning deaths occurring between May and August.

Epidemiology

The World Health Organization (WHO) defines drowning as "the process of experiencing respiratory impairment from the submersion/immersion in liquid." Drowning is one of the leading causes of death and disability in children under the age of 14 (see Figure 1). In fact, it is the second leading cause of accidental death in this population, with an estimated 1,100-1,400 deaths per year in the United States. Near drowning is even more frequent and accounts for at least 4,000 emergency department visits per year, with some estimating that the true incidence is two to 20 times higher due to children presenting to their pediatricians or urgent cares, or not seeking medical treatment, as well as underreporting.

There are a variety of sociodemographic circumstances that factor into drownings. The rates and mechanism of drowning vary with age, gender, and race. The highest rate of drowning is in the under five-year-old group, with a second smaller peak in adolescents and young adults. Infants are most likely to drown in a bathtub or small body of water, whereas children ages one to five most commonly drown in pools. As children get older and enter adolescence, there is an increased rate of open-body freshwater drownings. In terms of gender, up until roughly age 12, male children are twice as likely to die from drowning as female children. After this age, the difference increases to almost tenfold. A variety of factors may play a role in this staggering difference, including higher risk-taking and greater alcohol consumption by males in this age group. Finally, there continues to be racial disparities in drowning. This is most prevalent in the 10-12-year-old population, with a marked increase in the rate of African American male pool drownings as compared to other racial groups. This holds true even when socioeconomic factors are controlled for.



Source: Centers for Disease Control and Prevention

Figure 1: Intentional and unintentional deaths in children ages 1-14 years in 2014

Figure 2: Imaging showing a patient with Acute Respiratory Distress Syndrome (ARDS)

Pathophysiology

Clinically, drowning has often been described as occurring in stages. The first stage is marked by breath holding, panic, air hunger, and attempts to resurface. This is often followed by reflex inspiratory efforts, which lead to aspiration and/or involuntary laryngospasm resulting in hypercapnia, hypoxemia, and ultimately pulmonary or cardiopulmonary arrest. Unlike many traumatic events, drowning is often an eerily silent event in the young.

Pulmonary — Pulmonary injury and problems are the most frequently encountered and severe organ derangements in drowning patients. The basic pathology is hypoxemia and ischemia. Drowning causes abnormal surfactant production, leading to increased endothelial permeability, and resulting in increased intrapulmonary shunting. This causes oxygenation and ventilation insufficiency due to bronchospasm, atelectasis, aspirated material, decreased lung compliance, and ultimately may lead to Acute Respiratory Distress Syndrome (ARDS) (see Figure 2).

Cardiovascular — Dysrhythmias and cardiac dysfunction are not uncommon in drowning victims. The most commonly encountered are sinus bradycardia, but patients can present in ventricular fibrillation or asystole. Dysrhythmias are secondary to hypoxemia, acidosis, hypothermia, and electrolyte abnormalities. In patients initially presenting in cardiac arrest, only 5% will have an initial shockable rhythm.

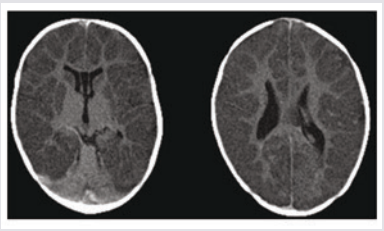


Figure 3: Cerebral edema post drowning

Neurological — The most frequent cause of death in drowning patients is secondary to a neurologic insult due to hypoxemia and ischemia. The principal determinant of outcome is the duration of hypoxemia/ischemia. Hyperventilation may also lead to hypocapnia, further decreasing cerebral blood flow and increasing neuronal injury. This ultimately leads to cerebral edema (see Figure 3) and increased intracranial pressure typically peaking around 24 hours. Initial Glasgow Coma Scale (GCS) scores of <5 and abnormalities on the initial CT scan are predictors of poor outcome and death. Limiting of the initial hypoxemia/ischemia as well as avoiding secondary insults of hypoxemia, hypocapnia, and ischemia may lead to improved outcomes. Severe neurologic sequelae is seen in 10-20% of near-drowning children.

Treatment

Prehospital — Because the outcome of drowning victims is related to hypoxemia, treatment is aimed at reducing this. Children should be rescued as soon as possible. Cervical spine should be immobilized in appropriate situations (history of or signs of trauma). If the patient is unresponsive with abnormal breathing, then basic life support (BLS) should be initiated with CPR. This should be initiated as early as possible to obtain normal breathing and oxygenation and reduce hypoxemia.

Hospital — The activation of a trauma alert is not standard and has been debated in the field. Traumatic injuries are absent in most patients and routine activation may divert resources. Whether a trauma alert is activated or not, evaluation should be thorough and methodical. The standard ABCs, or airway, breathing/oxygenation, and circulation, should be assessed and treated with additional attention for signs of trauma. Patients are often hypothermic and should be aggressively rewarmed. In severe cases, extracorporeal membrane oxygenation (ECMO) has been utilized for both rewarming as well as cardio-pulmonary support, but this is still somewhat controversial.

Prevention

Up to 90% of drowning victims are within 10 yards of safety at the time of drowning. Proper monitoring of young children is critical. Small children should never be left unattended around any body of water (pool, bathtub, lake, etc.). Be aware of streams, creeks, ponds, ditches, or any other bodies of water on or near your property. Standing water left in buckets, wading pools, bathtubs, toilets, and so on, can be dangerous to toddlers. Water safety classes may be beneficial but still do not replace adequate supervision. Increasing CPR training may be a useful secondary prevention method to reduce the hypoxemia associated with drowning.

Swimming pools should be enclosed by a four-sided fence that is at least five feet high and separates the pool area from the house. The fence gate should have a self-closing, self-latching mechanism and should be located on the side of the fence closest to the pool and out of reach of small children. Complete enclosure of a pool by a fence reduces pool drownings by 50%. Pool covers are an inadequate method alone. Approved personal floatation devices (PFDs) should be worn by all passengers in powered and unpowered watercraft, or by anyone who is unable to swim or is unsure of their swimming abilities when in and around water. "Water wings" are not a dependable flotation device and are no substitute for adult supervision of small children in and around water.

As warmer weather approaches, we have to be aware of drowning risks. Drowning continues to be one of the most frequent causes of death both in the United States and around the world. As numerous studies have shown, the majority of drownings are likely preventable. As members of not only the medical field, but also as parents and community members, it is our responsibility to educate, treat, and protect the children around us and in our communities.

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To Scan or Not to Scan? The Benefits and Drawbacks of the Pan-Scan in the Evaluation of Blunt Force Trauma

by James L. Patrick, MD, PhD

Computed tomography (CT) has become the workhorse in the evaluation of hemodynamically stable trauma patients. Since its inception, a tailored imaging approach became the standard of care. For example, a patient involved in a motor vehicle crash who experienced abdominal pain would get a CT of the abdomen and pelvis, along with plain film imaging of other anatomical regions, such as a chest x-ray for trauma screening. More recently, a whole-body CT (WBCT), or "pan- scan," approach has been adopted in the United States for patients who have appropriate mechanism of injury that places them at risk for unexpected injury. There has been a contentious debate about which imaging approach is the most appropriate and should be the standard of care. The purpose of this article is to discuss the pros and cons of WBCT in the context of blunt force trauma.

What Is Whole-Body CT and How Is it Performed?

WBCT involves dedicated images of the head, cervical spine, thorax, abdomen, pelvis, thoracic spine, and lumbar spine. Examination begins with a non-contrast head CT and cervical spine. Next is an arterial phase scan of the chest and upper abdomen. A portal venous phase study is then performed from the lower thorax to the deep pelvis. The biphasic study allows for the evaluation of vascular and non-vascular injury. Additionally, this helps to differentiate between contained and uncontained vascular injuries, such as pseudoaneurysms and arteriovenous fistulas versus active hemorrhage. Thoracic-lumbar spine images are generated from the source data. At UPMC, the images are divided into neuroradiology and body studies and sent to the appropriate division. UPMC is only one of two facilities in the United States where scans are interpreted by fellowship-trained subspecialized radiologists on a 24/7 basis.

Pros and Cons of Whole-Body CT

The most obvious and concerning problem associated with WBCT is the increase in radiation dose imparted to the patients. The overall dose from WBCT is approximately 1.5 times that of a conventional or standard protocol, in which patients receive a total of 24 versus 16 millisieverts (mSv), respectively.[1] Several studies have quantified the effective dose of radiation to trauma patients over varying periods of time during their hospital stay. Median exposure ranged between 22.7 and 40 mSv. Based on the National Academy's seventh report of biological radiation, in theory, this could lead to an additional 322 cancer deaths out of 100,000 people.[2] These excess mortality predictions are based upon a stochastic model and assume a linear relationship between exposure and cancer induction; therefore, there is no clear threshold below which radiation exposure is safe.

It is important to note that the age of the patient has a profound effect on their overall cancer risk. Pediatric and young adult populations are at a higher risk of developing lethal malignancy in the future than an older individual who receives the same dose of radiation. While there is no magical cutoff in which patients can be scanned with impunity, data suggests that after the age of 35, there is a reduced fatal cancer risk.[3]

While the initial cost of the WB protocol is higher, a large study evaluating the benefit-cost ratio of early intervention from WBCT results has not yet been performed. An additional concern with WBCT has been the discovery of incidental or false positive findings leading to further imaging and workup that may increase downstream costs.

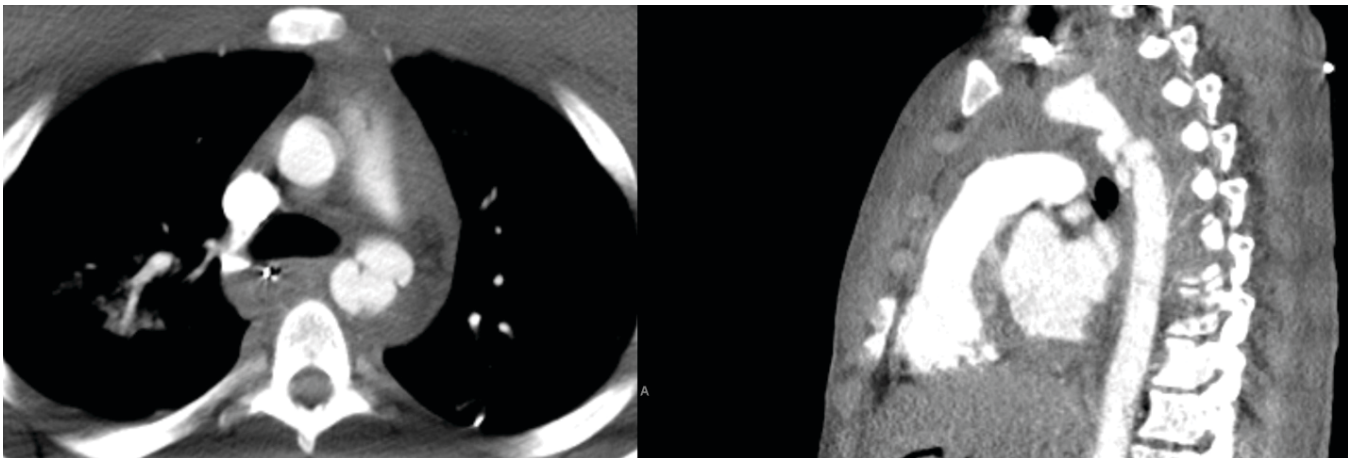

Figure 1: Young adult who reportedly fell from a seven-story window. Secular outpouching of the descending aorta and hemomediastinum consistent with aortic pseudoaneurysm.

The benefits of WBCT are fairly obvious. It is an extremely accurate and sensitive modality for the detection of both visceral and vascular trauma. It has a fast turnaround time with an opportunity for quick interpretation and necessary intervention. CT in general has reduced the need for exploratory surgery and has allowed for more successful utilization of non-operative management. This has decreased mortality and morbidity for the trauma patient. Also, WBCT can identify unexpected injuries in asymptomatic trauma patients requiring a change in management. In one study, 19% of the patients had a clinically significant abnormality resulting in a change in management.[4]

What Does the Literature Say?

A number of retrospective cohort studies and several meta-analyses have been conducted to determine the impact of WBCT on outcomes.[5,6] The general conclusion is that the WBCT group has an overall lower mortality rate than a selective scanning approach, although in some cases the design of the studies was brought into question. The REACT 2 study was a multi-center randomized controlled trial comparing the mortality benefit of WBCT versus a standard radiological workup. The conclusion was that immediate WBCT does not reduce in-hospital mortality when compared to the standard radiological workup, and because of increased radiation, future research should be performed on the selection of patients who would benefit from WBCT.[7] While this was the first randomized controlled study evaluating WBCT, there are several things to consider. There was only a slight increase in the radiation exposure for the WBCT group compared to the standard protocol (21.0 mSv versus 20.6 mSv, respectively); and while this was statistically significant, it is unclear whether it is clinically relevant. In addition, since the radiation doses were similar, this suggests that the patients randomized to standard protocol had an "almost" pan-scan performed. Additionally there is no clear analysis of other serious outcomes besides mortality, such as missed injuries that could change management or impact other outcomes.

Conclusions

There is clearly a need for additional studies to evaluate the benefits and drawbacks of WBCT, specifically large confirmatory studies looking at whether WBCT provides any decrease in mortality and morbidity. Additionally, studies of the benefit-cost ratio are needed to determine whether early diagnosis and treatment offset the initial increased cost of WBCT. Research is also needed on whether WBCT affects health care costs by identifying incidental findings that require further diagnostic examination. While these factors are germane to the expanded use of WBCT, the most important issue is the detection of CT findings that change management versus patient radiation dose. Therefore, it is important to identify the patients, specifically the young adults and pediatric population, who are at an increased risk from radiation exposure and to scan them more judiciously. Overall, however, WBCT provides a systematic and effective way to identify unexpected traumatic injury that changes clinical management and should be considered in symptomatic polytrauma patients or individuals with a history of significant mechanism of injury.

It is important to note that the studies discussed in this article were performed at verified trauma centers and the conclusions drawn cannot be applied to non-trauma centers. In fact, if a patient meets the physiological or mechanism of injury criteria for trauma center triage, CT imaging should be deferred until the patient has been transferred to the trauma center for proper evaluation and management. Furthermore, it should be noted that CT imaging is contra-indicated in hemodynamically unstable trauma patients who require immediate intervention rather than diagnostic testing, which may delay intervention.

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