# ETIOPATHOGENETIC ASPECTS AND OPTIMIZATION OF TREATMENT FOR ACUTE INTESTINAL INFECTIONS WITH HEMOCOLITIC SYNDROME IN CHILDREN

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### RELEVANCE

Acute intestinal infections accompanied by hemocolitic syndrome (acute bloody diarrhea, or dysentery) in children remain a significant global health challenge. Diarrheal diseases are a leading cause of pediatric morbidity and mortality worldwide, accounting for an estimated 444,000 deaths annually in children under 5 years of age . A substantial subset of these severe cases involve bloody diarrhea, which typically indicates invasive infection and carries higher risks of complications than non-bloody diarrhea. Globally, Shigella – the bacterium causing bacillary dysentery – is a primary etiologic agent of acute bloody diarrhea in young children and is responsible for a considerable portion of diarrheal deaths and illness episodes in this age group . Estimates suggest Shigella causes on the order of 75,000 deaths in children under 5 each year and hundreds of thousands of cases across all ages . Other pathogens such as Enterohemorrhagic Escherichia coli (EHEC), Campylobacter, and Entamoeba histolytica also contribute to pediatric hemocolitic syndrome, further underlining its global importance. Campylobacter infection, for example, is one of the most common causes of bacterial gastroenteritis worldwide and frequently leads to bloody diarrhea in young children . Acute bloody diarrhea not only can result in life-threatening dehydration and sepsis, but also may cause long-term effects such as malnutrition, growth faltering, or renal injury (in cases complicated by hemolytic-uremic syndrome). Given the substantial disease burden and the potential for severe outcomes, optimizing the understanding of pathogenesis and improving treatment strategies for hemocolitic syndrome in children is highly relevant to global child health.

**Keywords:** Acute intestinal infection; Hemocolitic syndrome; Bloody diarrhea; Dysentery; Children; Etiopathogenesis; Treatment optimization; Global health

### INTRODUCTION

Acute intestinal infections with hemocolitic syndrome refer to enteric infections that cause inflammation of the colon with bloody stool, commonly known as dysentery in clinical terms . This condition in children is most often associated with invasive bacterial pathogens that attack the colonic mucosa, leading to mucosal ulceration, bleeding, and systemic illness. The most prevalent etiologic agents include Shigella species (causing bacillary dysentery) and Shiga toxin-producing Escherichia coli (such as E. coli O157:H7, causing hemorrhagic colitis), with other contributors being Campylobacter jejuni, Salmonella (in some invasive diarrheal cases), and Entamoeba histolytica (causing amoebic dysentery). Among these, Shigella is identified as the leading cause of acute bloody diarrhea in children under 5, particularly in low- and middle-income countries . Globally, Shigella infection (shigellosis) has an enormous impact, with an estimated 188 million cases annually and approximately 164,000 associated deaths reported in earlier studies . Likewise, Campylobacter and EHEC infections are widespread across regions – Campylobacter is considered the most common bacterial cause of gastroenteritis worldwide,

frequently causing bloody diarrhea in young children  , and EHEC outbreaks have been documented on every inhabited continent due to contaminated food or water sources.

From a pathophysiological standpoint, hemocolitic syndrome is characterized by acute inflammatory damage to the colonic epithelium. Infections like shigellosis and EHEC trigger intense colonic inflammation through distinct mechanisms: Shigella invades the colonic mucosa and induces cell destruction and ulceration, whereas EHEC produces potent Shiga toxins that injure the vascular endothelium of the colon, leading to hemorrhage  . The resulting clinical picture typically includes frequent small-volume stools with blood and mucus, abdominal cramping, tenesmus (painful straining), and fever – features that distinguish dysentery from watery diarrheas. These infections can lead to severe dehydration, sepsis, or, in the case of Shiga toxin-producing organisms, hemolytic-uremic syndrome (HUS), which is a major cause of acute kidney failure in children.

The global significance of acute hemocolitic infections in children is further highlighted by their potential for outbreaks and the challenge of antimicrobial resistance. Epidemics of dysentery, such as those caused by Shigella dysenteriae type 1 in humanitarian crises, have historically resulted in high mortality. Meanwhile, increasing drug resistance in Shigella and other enteric bacteria is undermining standard treatments  , necessitating an evidence-based reassessment of optimal therapeutic approaches. This article aims to examine the etiopathogenetic aspects of acute intestinal infections with hemocolitic syndrome in children and to evaluate strategies for optimizing treatment outcomes. We take a global perspective, integrating data from diverse regions and recent clinical evidence, to provide recommendations for clinicians managing pediatric dysentery and to identify priorities for future research.

## MATERIALS AND METHODS

Study Design: This work is structured as a comprehensive narrative review supplemented by analysis of epidemiological data and clinical studies. We conducted a literature search focusing on pediatric acute bloody diarrhea (hemocolitic syndrome) to gather information on causative pathogens, pathogenesis, clinical course, and treatment outcomes. Sources included international health organization reports, global burden of disease studies, clinical practice guidelines, and peer-reviewed research articles (including randomized trials and meta-analyses). No new patient data were collected for this review; rather, published data from multiple regions were analyzed to ensure a global scope.

Patient Population: The review emphasizes children (primarily under 5 years old, but including up to adolescence) suffering from acute intestinal infections with bloody diarrhea. This population is of interest because young children bear the highest incidence of severe diarrheal disease and are particularly vulnerable to complications like dehydration and HUS. Where available, data from both developing countries (where dysentery is often endemic) and developed countries (where sporadic outbreaks of EHEC or Campylobacter occur) were included to contrast etiological patterns and management practices.

Diagnostic Methods: We reviewed diagnostic approaches for identifying the etiologic agents of hemocolitic syndrome. These include conventional stool culture techniques for bacterial pathogens (e.g., Shigella, Salmonella, Campylobacter, pathogenic E. coli), stool microscopy and antigen testing for parasitic causes (e.g., E. histolytica), and newer rapid diagnostics. In many references, stool culture is considered the gold standard for dysentery diagnosis and for antimicrobial susceptibility testing  . We note that EHEC diagnosis often requires special media or toxin assays (such as sorbitol-MacConkey agar culture for O157 or immunoassays/PCR for Shiga toxin genes) given that routine stool culture may not detect non-

sorbitol-fermenting E. coli . Molecular multiplex PCR panels are increasingly used in high-resource settings to rapidly identify a broad range of enteropathogens, though their accessibility in low-resource settings is limited . The review also considers clinical and laboratory indicators used to assess disease severity (e.g., presence of fever, number of blood stools, signs of dehydration, blood tests indicating renal impairment or hemolysis in suspected HUS) as part of the diagnostic workup.

Treatment Approaches: We compiled data on both supportive care and specific antimicrobial therapy for acute bloody diarrhea in children. Supportive management (oral or intravenous rehydration, electrolyte correction, and nutritional support) is universally regarded as the cornerstone of treatment for acute diarrheal illness . We identified guidelines for antibiotic use in dysentery, recognizing that appropriate antimicrobial therapy can shorten illness duration and reduce pathogen transmission in bacterial dysentery . However, antibiotic choices must account for the causative organism and local resistance patterns. Our methods involved comparing recommendations from the World Health Organization (WHO), Infectious Diseases Society of America (IDSA), and other regional pediatric protocols on when and what antibiotics to administer. We also reviewed evidence on adjunct therapies such as zinc supplementation (widely recommended in childhood diarrhea to improve outcomes ), probiotics, and anti-motility agents (the latter generally contraindicated in dysentery). Finally, we examined outcome data from clinical trials and observational studies, including metrics like duration of diarrhea, time to clearance of blood from stool, complication rates (e.g., incidence of HUS or sepsis), and case fatality rates, to gauge the effectiveness of various treatment strategies.

## ANALYSIS AND RESULTS

Etiological spectrum of hemocolitic syndrome in children - Our analysis confirms that a limited set of pathogens are responsible for the majority of acute hemocolitic (bloody diarrheal) infections in children, although the prevalence of each can vary by region and setting. The major etiologic agents identified include:

Shigella species (Bacillary Dysentery): Shigella is the leading cause of dysentery in young children worldwide. Four species exist (S. dysenteriae, S. flexneri, S. boydii, S. sonnei), with S. flexneri predominating in many low-income regions and S. sonnei more common in industrialized countries . S. dysenteriae type 1, though less frequently encountered, is historically known for causing severe epidemics of dysentery with high mortality. Shigella spreads via the fecal-oral route, often through contaminated water or food, and extremely low inoculum (as few as 10 organisms) can cause infection . Clinically, shigellosis presents with high fever, abdominal cramps, and frequent small-volume stools that contain blood and mucus. Without treatment, illness typically lasts about a week, but severe cases can lead to dehydration or sepsis, especially in malnourished children. In our review of global data, Shigella was consistently identified as a dominant cause of acute bloody diarrhea in children under 5; for instance, the multi-country GEMS study found Shigella to be a top pathogen causing moderate-to-severe diarrhea in toddlers . Importantly, Shigella infection contributes significantly to child mortality: recent burden estimates attribute roughly 13–17% of all diarrhea-related deaths in under-5 children to shigellosis .

Enterohemorrhagic E. coli (EHEC): EHEC, especially serotype O157:H7 and certain non-O157 strains, is a notable cause of bloody diarrhea outbreaks, often linked to foodborne transmission (undercooked beef, unpasteurized milk, contaminated produce). These bacteria produce Shiga toxins (Stx) analogous to S. dysenteriae toxins . Unlike Shigella, EHEC typically do not invade the intestinal lining deeply; instead, they attach to the colonic epithelium

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and secrete toxins that damage the intestinal blood vessels, leading to hemorrhagic colitis. Children infected with EHEC present with severe abdominal pain and bloody diarrhea that may be initially non-bloody but becomes frankly bloody within 1–2 days   . Fever is often absent or low-grade. A feared complication of EHEC infection is hemolytic-uremic syndrome (HUS), characterized by hemolytic anemia, thrombocytopenia, and acute kidney injury. Our findings indicate that HUS develops in a significant minority of pediatric EHEC cases. According to the WHO, up to about 10% of children with STEC (Shiga toxin-producing E. coli) infection may progress to HUS   , and this complication is the leading cause of acute renal failure in young children. HUS carries a mortality of several percent and risk of long-term renal sequelae among survivors  . The propensity for severe systemic complications makes EHEC infections particularly concerning despite their lower incidence compared to Shigella in many regions.

Campylobacter jejuni and related species: Campylobacter is a common bacterial pathogen causing gastroenteritis in all age groups. In children under 2 years, especially in developing countries, Campylobacter infections are frequent and can cause dysentery-like illness with fever and bloody diarrhea   . The organism is typically foodborne (found in undercooked poultry, unpasteurized milk, etc.) and is also zoonotic. While many Campylobacter infections result in watery diarrhea, a substantial proportion present with visible blood and leukocytes in stool due to the bacterium's ability to invade and induce inflammation in the colon. The illness usually lasts under one week. Severe complications are relatively rare but can include bacteremia or post-infectious sequelae like Guillain-Barré syndrome (an autoimmune paralysis) in a small fraction of cases   . Our literature review noted that Campylobacter is recognized as one of the four key global causes of diarrheal disease, and in some settings it rivals or exceeds Shigella as a cause of pediatric diarrhea (often identified when broad stool diagnostic methods are employed)   . However, because Campylobacter often causes illness that is self-limited and not routinely tested for in some regions, its contribution to hemocolitic syndrome may be underappreciated.

Non-typhoidal Salmonella (NTS): Invasive Salmonella infections (e.g., Salmonella enteritidis, S. typhimurium) can cause a spectrum of illness from gastroenteritis to bacteremia. NTS are a less frequent cause of bloody diarrhea than Shigella or Campylobacter, but in young children they can produce an inflammatory diarrhea sometimes with blood and mucus. Typically, Salmonella diarrhea is watery; frank dysentery may indicate a particularly severe colitis or co-infection. Because NTS often penetrate beyond the intestinal mucosa, they can cause systemic infection (fever, bloodstream infection) more commonly than other diarrheal bacteria. Fatal outcomes from NTS are usually due to invasive disease rather than the diarrheal component. In our global perspective, NTS is an important consideration primarily in areas with high incidence of foodborne disease or in immunocompromised hosts. It is noteworthy that Salmonella and Campylobacter together account for a significant proportion of diarrhea hospitalizations in high-income countries, whereas Shigella and EHEC are more often diagnosed in the context of outbreaks or travel.

Entamoeba histolytica (Amoebic Dysentery): E. histolytica, a protozoan parasite, causes amoebiasis which can manifest as chronic or acute dysentery. Amoebic colitis results from the parasite invading the colonic wall, leading to ulcers and bloody mucoid diarrhea, often with abdominal pain and tenesmus. While amoebic dysentery is more common in older children and adults, it is also seen in pediatric populations in areas with poor sanitation and hygiene. In this review, we found that amoebiasis remains a prevalent cause of bloody diarrhea in many tropical regions. E. histolytica infection is estimated to infect tens of millions worldwide annually,

though many cases are asymptomatic or mild    . Severe amoebic dysentery can mimic bacillary dysentery clinically; however, high fever is less common and the onset may be more insidious. Importantly, E. histolytica can cause complications such as colonic perforation or liver abscesses. Its inclusion in the differential diagnosis of hemocolitic syndrome is crucial in endemic areas or when initial bacterial cultures are negative, since treatment differs (anti-parasitic drugs rather than antibiotics used for bacteria).

In addition to the above, other less common causes of acute hemocolitic syndrome in children include Clostridioides difficile (post-antibiotic or hospital-associated colitis, which can occur in pediatric patients and cause pseudomembranous colitis with bloody stools), Yersinia enterocolitica (which can cause bloody diarrhea and mesenteric lymphadenitis, often in older children), and certain viral infections (though most viral diarrheas, like rotavirus, are non-bloody; adenovirus or cytomegalovirus in immunocompromised hosts can occasionally cause hemorrhagic colitis). It is also important to note that non-infectious conditions (like new-onset inflammatory bowel disease) can initially present with similar symptoms in children, though these are differentiated by chronicity and other clinical context.

Pathogenesis and clinical features - Despite the variety of pathogens, there are common pathogenic pathways that lead to colonic inflammation and bleeding in hemocolitic syndrome. Typically, the causative organisms either invade the colonic epithelium or produce cytotoxins (or both), inciting a strong inflammatory response:

In shigellosis, pathogenesis involves Shigella bacteria invading the colonic mucosa through M-cells in the Peyer's patches, then spreading cell-to-cell. Shigella triggers macrophage apoptosis and induces a cascade of inflammatory cytokines (IL-1, IL-8) that recruit neutrophils to the colon    . The intense neutrophilic response and direct bacterial cytotoxicity lead to mucosal ulcerations and exudation of blood and pus into the intestinal lumen. Some Shigella strains (especially S. dysenteriae type 1) produce Shiga toxin, which can exacerbate tissue damage and cause systemic effects like HUS    . Clinically, after an incubation of 1–4 days, children develop high fever and cramps followed by frequent small-volume diarrhea with blood and mucus. The stools often contain numerous polymorphonuclear leukocytes on microscopy, reflecting the acute colitis. Children may also experience rectal pain and prolapse (due to severe tenesmus), and in severe cases neurological manifestations like seizures can occur (sometimes attributed to the Shiga toxin or electrolyte disturbances). Without treatment, the illness can last about a week or more; with effective therapy, symptoms usually improve within 48–72 hours. Complications of shigellosis can include dehydration, electrolyte imbalances, and, in malnourished children, an increased risk of bacteremia or persistent diarrhea. Mortality rates in treated shigellosis are typically low (<1%), but in epidemics or without access to care, case-fatality can be substantial.

In EHEC/STEC infection, the bacteria colonize the colon without significant invasion. They possess a pathogenicity island (the locus of enterocyte effacement) that allows them to attach tightly to intestinal epithelial cells and efface microvilli. The primary damage comes from Shiga toxins (Stx1, Stx2) released by the bacteria, which injure endothelial cells in the intestinal capillaries, leading to hemorrhage and an inflammatory response. The result is hemorrhagic colitis – copious bloody diarrhea often described as "all blood, no stool" in severe cases    . Systemically, absorbed toxin can trigger HUS by damaging the endothelium in the renal glomeruli and other organs. Notably, antibiotic-induced bacterial stress can increase toxin release (an SOS response in the bacteria)    . Clinically, EHEC infection has an incubation of about 3–4 days. Young children present with abdominal pain and watery diarrhea that becomes bloody.

There is usually little or no fever, which, along with the severe pain, may initially suggest surgical abdomen (like intussusception or appendicitis) until diarrhea ensues    . If HUS develops, it typically does so about 1 week after diarrhea onset: children will show pallor (from hemolytic anemia), decreasing urine output, and petechiae or bleeding (from thrombocytopenia). In this review, we found that overall HUS occurs in roughly 5–15% of pediatric EHEC infections, with higher rates in infants and in outbreak settings    . This aligns with surveillance data indicating ~6% average in some cohorts and up to 15% in under-5 children in certain outbreaks    . The possibility of life-threatening HUS makes early recognition of EHEC crucial so that supportive measures (e.g. hydration, avoidance of precipitating factors) can be maximized.

In Campylobacter and Salmonella infections, the pathogenesis involves bacterial invasion of the intestinal epithelium and toxin production to a lesser degree. Campylobacter jejuni invades the small and large intestinal mucosa, causing an acute inflammatory response similar to Shigella. Salmonella can invade intestinal cells and also survive within macrophages, leading to a mix of mucosal and systemic infection. These infections usually cause fever at onset, with Campylobacter often producing high fever and dysenteric stools. The presence of blood in stool in Campylobacter infection correlates with more extensive colonic involvement. Both organisms can disseminate: Salmonella especially can cause bacteremia in young or immune-compromised children, and Campylobacter can rarely do so as well. Reactive arthritis is a known post-infectious complication of Campylobacter in a small percentage of cases.

In Entamoeba histolytica (amoebic dysentery), the pathogenesis is distinct in that a protozoan parasite is involved. Ingestion of E. histolytica cysts (from fecally contaminated water/food) leads to release of trophozoites in the gut, which can adhere to and dissolve colonic mucus and epithelium using proteolytic enzymes. Trophozoites can ulcerate the colonic wall, creating classic "flask-shaped" ulcers that bleed. The inflammatory response is generally less neutrophil-rich than in bacterial dysentery; in fact, amoebic dysentery can sometimes show fewer fecal leukocytes despite bloody stool. Symptoms may be more gradual in onset and protracted. If the parasite invades blood vessels, it can spread to the liver and form abscesses. The clinical differentiation of amoebic vs. bacillary dysentery can be challenging, but amoebiasis may present with longer duration, lower grade fever, and a history of travel or residence in endemic areas. Stool examinations or antigen tests help identify the parasite.

Overall, children with acute hemocolitic syndrome present with signs of colitis: frequent bowel movements with blood/mucus, pain, and urgency. Physical examination often reveals dehydration (dry mucous membranes, reduced skin turgor) if intake hasn't matched losses, and possibly abdominal tenderness. High fever is more common in invasive bacterial causes (e.g. Shigella, Campylobacter), while mild or absent fever is noted in toxin-driven cases like typical EHEC. In any child with bloody diarrhea, close monitoring for complications is warranted. Our review reinforces that timely identification of the cause can influence management – for instance, if EHEC is suspected, one should vigilantly watch for HUS signs and avoid certain treatments, whereas if Shigella is confirmed, prompt antibiotic therapy is indicated to shorten disease and reduce transmission.

Diagnostic findings - Accurate diagnosis of the specific etiologic agent in hemocolitic syndrome is ideal but not always achievable in resource-limited settings. The analysis of diagnostic methods yielded the following key points:

Stool Culture and Microscopy: Stool culture remains the definitive diagnostic test for bacterial dysentery. It allows identification of Shigella, Salmonella, Campylobacter, and E. coli strains (though EHEC O157 requires special culture media). In practice, when a child presents

with dysentery, stool culture should be performed whenever possible to guide therapy and public health responses . Microscopic exam of stool can support the diagnosis: the presence of numerous fecal leukocytes (pus cells) and erythrocytes is typical in bacterial colitis (e.g., Shigella, Campylobacter), whereas their absence makes invasive infection less likely. For E. histolytica, stool microscopy may show cysts or trophozoites (sometimes with ingested red blood cells inside them), but modern antigen tests or PCR are more sensitive.

Rapid Antigen or Toxin Tests: Many labs use immunoassays to detect Shiga toxin in stool, which provides a rapid presumptive diagnosis of STEC infection. If positive, this alerts clinicians to the risk of HUS even before culture confirmation. Similarly, antigen tests for Entamoeba histolytica in stool can distinguish it from non-pathogenic amoebae. There are also point-of-care tests for Shigella (though not widely used yet) and common viruses (to rule out viral diarrhea in bloody cases where sometimes co-infection or another cause might be present). Our review found that implementation of a combined approach (culture plus antigen/PCR) increases pathogen yield significantly, as reported in hospital-based studies in both high-income and developing countries.

Molecular Multiplex PCR: In recent years, multiplex PCR panels that detect a wide array of enteropathogens (bacteria, viruses, protozoa) from stool have become available. These tests can identify Shigella, EHEC, Campylobacter, Salmonella, Yersinia, and E. histolytica among others in a single assay. They have high sensitivity and rapid turnaround. For example, a PCR-based study might show that a child's bloody diarrhea is due to Campylobacter where routine culture might have missed it. However, cost and technical requirements limit widespread use in low-resource settings.

Blood Tests and Other Investigations: While diagnosis rests on stool analysis, certain blood test findings are noteworthy. A complete blood count often shows elevated white blood cell count with neutrophil predominance in bacterial dysentery. Markers of inflammation (C-reactive protein) are typically high. If HUS is developing, blood tests will reveal hemolytic anemia (low hemoglobin with fragmented red cells on smear), thrombocytopenia, and rising blood urea nitrogen/creatinine indicating renal injury. Electrolytes may show abnormalities like acidosis or low potassium if diarrhea has been prolonged. In protracted or unclear cases, clinicians sometimes perform sigmoidoscopy, which in dysentery shows an inflamed, friable mucosa with punctate ulcers, and can allow biopsy to distinguish causes (though this is rarely needed acutely).

The outcome of our analysis underscores the importance of at least obtaining a stool culture in cases of pediatric hemocolitic syndrome, as recommended by international guidelines . Not only does this confirm the diagnosis, but also allows antibiotic susceptibility testing – crucial given rising resistance in organisms like Shigella. In resource-poor settings where culture is not available, the diagnosis is often syndromic: any child with visible blood in diarrhea is presumed to have Shigella infection and treated empirically for it, as per WHO guidelines, because Shigella is the most likely cause and effective treatment exists. This approach prioritizes immediate therapy over aetiologic precision, but risks missing other diagnoses (e.g., amoebiasis or EHEC where management would differ). Therefore, improving access to diagnostics is part of optimizing outcomes for these children globally.

Treatment outcomes and therapeutic considerations - The management of acute intestinal infections with hemocolitic syndrome in children hinges on two main components: aggressive supportive care and appropriate antimicrobial (or antiparasitic) therapy when indicated. The goal is to promptly stabilize the child, eliminate the pathogen, and prevent

complications. We synthesized evidence from clinical trials, meta-analyses, and guidelines to determine best practices:

Supportive Care: All sources reviewed concur that rehydration and supportive measures are the first priority in treating acute diarrhea, including dysentery . Dehydration is a common immediate threat due to fluid losses. Oral rehydration therapy (ORT) using Oral Rehydration Salts solution is highly effective for mild to moderate dehydration and can be administered in most cases; intravenous fluids are reserved for children who cannot drink or who have severe dehydration or shock. WHO guidelines emphasize that even children with dysentery should receive ORT or IV fluids as needed, alongside continued feeding to mitigate malnutrition . In hemocolitic cases, rehydration may be somewhat more challenging if there is frequent small stool output, but careful monitoring and frequent small-volume administration are effective. Additionally, zinc supplementation (20 mg per day for 10–14 days for children over 6 months, 10 mg for infants) is recommended in all childhood diarrheal episodes, dysentery included, as it has been shown to shorten the duration of diarrhea and reduce early recurrence . Our review supports this recommendation: multiple studies and a Cochrane review have demonstrated improved outcomes with zinc, likely due to improved mucosal recovery and immune function. Nutritional support is also crucial – continued breastfeeding in infants and resuming age-appropriate diet early (within the limits of the child's tolerance) help prevent further weight loss and support healing of the gut.

Antimicrobial Therapy: The use of antibiotics (or antiparasitic drugs for amoebiasis) in hemocolitic syndrome is a critical factor that can drastically alter outcomes. We found that for bacterial causes of dysentery, timely antimicrobial treatment leads to faster clinical cure, shorter duration of fecal shedding of the pathogen, and reduced risk of severe sequelae. A meta-analysis of antibiotics for dysentery in children concluded that effective antibiotics significantly reduce the duration of bloody diarrhea (by approximately 2 days on average) and the duration of pathogen carriage in stool . Below we summarize optimal treatment by pathogen:

Shigella: Antibiotic therapy is indicated for confirmed or strongly suspected shigellosis in children, except perhaps very mild cases, because it both hastens recovery and curtails transmission . WHO and various national guidelines have for decades recommended antimicrobial treatment for dysentery (presumed Shigella infection) in all children. The choice of antibiotic depends on local resistance patterns. Shigella has developed widespread resistance to many first-line drugs (ampicillin, trimethoprim-sulfamethoxazole) in many regions, so those are ineffective in many cases. According to our literature review and current recommendations, azithromycin (a macrolide antibiotic) has emerged as a preferred first-line oral agent for pediatric shigellosis in many settings due to its efficacy and convenient dosing . A randomized controlled trial demonstrated an 82% clinical success rate with a 3-day azithromycin regimen in children, which was comparable to fluoroquinolone therapy . Fluoroquinolones (such as ciprofloxacin) are highly effective against Shigella and are recommended first-line for adults; they are also recommended by WHO for children in certain circumstances because of their potent activity . However, due to concerns about side effects in children, many clinicians reserve fluoroquinolones for cases where alternatives are not available or the strain is resistant to other agents. In practice, ciprofloxacin (15–20 mg/kg twice daily) for 3 days is still used in pediatric dysentery in some low-income countries as a pragmatic choice, and studies have found it to be generally safe and effective in children . Third-generation cephalosporins (like ceftriaxone or cefixime) are also important options: ceftriaxone (intravenously or intramuscularly for 2–5 days) is often used for hospitalized severe cases or infants, and oral

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cefixime is used in South Asia as first-line in areas with high resistance to other drugs . Pivmecillinam is another drug (a beta-lactam) used in some regions (e.g., Bangladesh, parts of Europe) for Shigella. The key is that the antibiotic should be tailored to susceptibility if known – our review highlighted rising instances of multidrug-resistant Shigella (including strains resistant to azithromycin and extended-spectrum beta-lactams) which complicate therapy . In extreme cases of extensively drug-resistant Shigella, combinations like carbapenems or colistin have been used as reported in outbreak settings , but this is fortunately rare. For typical cases, successful treatment results in defervescence and improvement of stools within 48 hours. If there's no improvement, it raises possibility of resistance, incorrect diagnosis, or complications.

EHEC/STEC: In stark contrast to shigellosis, antibiotic therapy is not recommended for EHEC infections. Our analysis reaffirms that giving antibiotics in the setting of EHEC can increase the risk of HUS, presumably by causing greater release of Shiga toxin when bacteria are killed under stress . Supportive care is the mainstay for EHEC – maintaining hydration, monitoring and managing pain, and avoiding anti-motility drugs. If an EHEC infection is suspected (e.g., bloody diarrhea without fever during an outbreak of O157 or pending stool toxin test results), clinicians should withhold antibiotics. The WHO specifically notes that antibiotics should not be part of STEC diarrhoea treatment and may heighten HUS risk . Empirical antibiotic treatment of dysentery, therefore, poses a dilemma: one does not want to treat EHEC with antibiotics, yet early on it may be indistinguishable from shigellosis. In practice, if a child appears very ill and dysentery is presumed to be Shigella, antibiotics (like a third-gen cephalosporin) might be started but should be discontinued if EHEC is confirmed. Fortunately, most EHEC infections in children will resolve spontaneously within a week or so with proper supportive care. During this period, vigilant monitoring for HUS is essential. This includes daily checks of urine output, weight (fluid status), blood pressure, and possibly blood tests for hemoglobin, platelets, and renal function in the days following the diarrhea. Early signs of HUS should prompt immediate hospitalization and specialist care (including renal dialysis if needed). There is ongoing research into therapies that might interrupt the pathogenesis of HUS (for example, monoclonal antibodies against Shiga toxin or complement inhibitors in early HUS), but none are standard care as of yet. The key point remains: for EHEC, supportive care is the only proven management, and outcomes are generally good if HUS does not occur. The case-fatality rate in pediatric EHEC colitis is low (<5%) unless complicated by HUS , which itself carries a higher fatality.

Campylobacter: Campylobacteriosis in children is often self-limited, but antibiotics can shorten the illness course, especially if given early. The recommended treatment for Campylobacter dysentery is a macrolide antibiotic – typically erythromycin or azithromycin for 3 days. This has been shown to reduce the duration of fecal shedding and symptoms. Many guidelines advise treating moderate to severe Campylobacter infections (high fever, bloody stools, or prolonged illness) with antibiotics, while mild cases can be observed. Fluoroquinolones are also effective against Campylobacter, but their use in young children is limited. In our review, treating Campylobacter was not a major focus in the literature because it is often not identified immediately; however, given its prevalence, some argue for empiric macrolide coverage in a child with dysentery in regions where Campylobacter is common. Clinicians should weigh this based on local epidemiology. Notably, Campylobacter resistance to fluoroquinolones is widespread (due to use in animal agriculture and in adults), but macrolides remain effective in most cases.

Non-typhoidal Salmonella: Antibiotics are usually not indicated for uncomplicated Salmonella gastroenteritis in immunocompetent hosts, as they do not significantly shorten diarrhea and may prolong Salmonella carriage. However, in infants (<3 months), in children with immune suppression, or if there are signs of invasive disease (high fever, bloodstream infection), antibiotic therapy is recommended. Options include third-generation cephalosporins (e.g., ceftriaxone) or amoxicillin/Trimethoprim-sulfamethoxazole if susceptible. Since it is often not known initially whether a bloody diarrhea is due to Salmonella or Shigella, clinicians might cover for Shigella; if culture later shows Salmonella, antibiotics can be stopped (unless criteria for treatment are met). The outcome of treated vs untreated Salmonella colitis in otherwise healthy children is usually similar, as most recover with supportive care alone. Thus, the mainstay here is again hydration and nutrition, with antibiotics reserved for complicated cases.

Entamoeba histolytica: Amoebic dysentery requires anti-parasitic treatment. The standard is metronidazole (or tinidazole) to eradicate the invasive trophozoites, followed by a luminal agent such as iodoquinol or paromomycin to clear residual cysts in the intestine (to prevent relapse and transmission). Metronidazole for 7–10 days yields high cure rates for amoebic colitis. In children with bloody diarrhea in endemic areas, if initial bacterial cultures are negative or if amoebic trophozoites are seen in stool, anti-amoebic therapy should be initiated. Co-infection is possible, so sometimes both antibiotics and metronidazole are given when diagnosis is uncertain. Our review did not find new trials altering the longstanding regimen for amoebiasis, but it is worth noting that without appropriate therapy, amoebic dysentery can become chronic or lead to complications like liver abscess which carry significant morbidity.

Adjunctive Therapies and Support: Beyond rehydration and antimicrobials, a few additional measures influence outcomes: Antipyretics and analgesics: High fever and abdominal cramping can cause distress in a child with dysentery, so paracetamol (acetaminophen) is often used for fever and pain relief. Nonsteroidal anti-inflammatory drugs (NSAIDs) are generally avoided due to risk of kidney injury especially if dehydration is present (important when HUS is a risk). Avoidance of anti-motility agents: It is strongly advised not to use loperamide or other anti-diarrheal medications in children with bloody diarrhea . These drugs can worsen the condition by retaining toxins and invasive organisms in the colon, and have been associated with toxic megacolon in Shigella infections . Our review reinforces that anti-motility agents are contraindicated in pediatric dysentery and that the focus should be on clearance of the pathogen rather than symptomatic slowing of stool frequency.

Probiotics: Some studies of probiotics in acute diarrhea show modest reduction in duration, particularly in viral diarrhea. In dysentery, evidence is less clear. Certain probiotics (like Lactobacillus rhamnosus GG or Saccharomyces boulardii) might help restore gut flora after infection, but they do not replace antibiotics for invasive bacterial infections [4]. They are generally safe except in severely immunocompromised patients. This review did not find conclusive data to recommend routine probiotic use in bloody diarrhea, but it could be considered as an adjunct after the acute phase.

Monitoring and managing complications: For severe cases, especially those hospitalized, careful monitoring is key. In Shigella dysentery, one must watch for signs of perforation (very rare; would present with acute abdominal signs) or sepsis (persistent high fever, lethargy, etc.). In EHEC, as noted, monitoring for HUS for at least a week after diarrhea onset is critical. If HUS occurs, management includes dialysis for renal failure, blood transfusions for anemia, and other supportive care in an intensive care setting. Neurologic complications in HUS (seizures, etc.) may require specialized care. The prompt involvement of pediatric nephrologists and critical care

can improve HUS outcomes. Our findings indicate that with good supportive care, the majority of children with HUS survive, although about half may be left with some degree of kidney impairment long-term   .

Outcomes: When optimal treatment is provided, the prognosis for acute hemocolitic infections in children is generally favorable. For example, with appropriate antibiotic therapy, shigellosis usually resolves within a few days and mortality is well under 1%. Even in resource-limited settings, the widespread use of ORT and antibiotics since the late 20th century has drastically reduced dysentery fatalities compared to historical levels. However, in the absence of treatment, dysentery can have a high mortality rate, particularly S. dysenteriae epidemics which historically saw case-fatality rates of 5–15% in children. EHEC infections have an overall mortality below 5% in developed healthcare systems, but HUS (which occurs in up to 1 in 10 cases) carries a higher mortality (~3–5% as per WHO data) and morbidity. Campylobacter and nontyphoidal Salmonella diarrheas are rarely fatal in otherwise healthy children if fluid losses are managed, though those that progress to bacteremia can be life-threatening without antibiotics. Amoebic dysentery, if untreated, can smolder and contribute to malnutrition and growth delays, and rarely can cause acute emergencies like fulminant colitis. With proper therapy, amoebiasis has a good outcome, and liver abscesses (the main invasive complication) respond well to metronidazole in most cases.

Our review also identified antimicrobial resistance as a growing factor that may impact outcomes. Multidrug-resistant Shigella strains (including those resistant to fluoroquinolones and azithromycin) have been reported and are associated with longer illness durations and increased risk of treatment failure   . This underscores the need for culture and sensitivity testing whenever possible, as well as the development of new treatments or vaccines [5]. The emergence of such strains in both developing and developed countries (often associated with international travel or specific transmission networks) is concerning. Similarly, increasing resistance in Campylobacter and Salmonella could complicate future management.

In summary, the results of this comprehensive analysis indicate that evidence-based interventions – prompt rehydration, judicious use of effective antibiotics (or antiparasitics), and careful monitoring – dramatically improve the outcomes of children with acute hemocolitic syndrome. Mortality and complication rates are low when these measures are implemented in a timely fashion. Conversely, delays in treatment or mismanagement (e.g., untreated dehydration, use of contraindicated drugs, inappropriate antibiotic choices) can lead to preventable deaths or sequelae. Therefore, optimizing treatment protocols and ensuring they are applied in all healthcare settings remains a priority in global child health.

**CONCLUSION AND RECOMMENDATIONS**

Acute intestinal infections with hemocolitic syndrome in children represent a serious global health concern due to their prevalence and potential for severe outcomes. This review highlights that Shigella species are the predominant etiologic agents of pediatric dysentery worldwide, with EHEC, Campylobacter, and other pathogens also contributing significantly. The etiopathogenesis involves invasive or toxin-mediated colonic injury, leading to the characteristic bloody diarrhea and systemic manifestations. Encouragingly, the vast majority of children can recover fully if they receive appropriate and timely treatment. Key elements of effective management include aggressive rehydration, nutritional support, and targeted antimicrobial therapy when indicated. We found that adherence to established treatment guidelines – such as administering antibiotics for Shigella and other invasive bacterial infections, while avoiding them in suspected EHEC – is critical for optimizing outcomes. In addition, adjunct measures like

zinc supplementation have a proven benefit in shortening illness duration. However, challenges remain, notably the rise of antibiotic-resistant strains and the limited diagnostic capabilities in many high-burden regions, which can delay appropriate care. There is a clear need for continued efforts to improve sanitation and preventive measures (to reduce disease incidence), as well as investments in healthcare infrastructure to manage cases effectively when they occur.

Recommendations for clinical practice: Based on the evidence reviewed, we propose the following best-practice recommendations for the management of acute hemocolitic syndrome in pediatric patients:

Early and aggressive rehydration: Assess dehydration in every child with bloody diarrhea and initiate ORS or IV fluids promptly. Do not delay rehydration while waiting for other interventions. Continue feeding (or breastfeeding) during diarrhea episodes to prevent malnutrition.

Obtain stool diagnostics whenever feasible: Perform stool culture and microscopy in cases of bloody diarrhea to confirm the causative agent and guide specific therapy. If available, use rapid tests (e.g., Shiga toxin assays) to identify EHEC, and test for E. histolytica antigen in endemic areas.

Empiric antimicrobial therapy for likely bacterial dysentery: In a child with acute bloody diarrhea and systemic illness (fever, etc.), begin empiric antibiotic treatment targeting Shigella after collecting stool for culture, except if an STEC infection is strongly suspected (such as during a known EHEC outbreak). Appropriate first-line choices include azithromycin for children, or a third-generation cephalosporin in severe hospitalized cases, adjusting once culture results are known. Avoid empiric use of drugs with high resistance in the region (e.g., TMP-SMX or ampicillin in many places).

Avoid antibiotics in suspected EHEC cases: If clinical and epidemiologic clues point to enterohemorrhagic E. coli (for example, bloody diarrhea without fever in a cluster of cases, or a positive Shiga toxin test), refrain from giving antibiotics and manage supportively. Provide close follow-up for signs of HUS for at least 7–10 days after onset.

Use antiparasitic therapy when indicated: If amoebic dysentery is diagnosed (or cannot be ruled out in a child from an endemic region), treat with metronidazole (appropriate pediatric dosing) followed by a luminal agent, even if bacterial causes are also being covered.

Adjunct therapy: Administer zinc supplements to all children with acute diarrhea (including dysentery) for 10–14 days as per WHO recommendations to promote intestinal recovery. Consider probiotics as an adjunct after acute phase, recognizing the evidence is not definitive for dysentery but they may aid gut flora restoration.

No anti-diarrheal drugs: Do not use loperamide or other anti-motility agents in children with bloody diarrhea, due to the risk of worsening the illness or precipitating toxic megacolon or HUS.

Monitoring and supportive measures: Monitor vital signs, urine output, and neurological status in hospitalized cases. Manage fever and pain with appropriate doses of acetaminophen. Involve pediatric specialists early if complications like HUS or sepsis are developing. Ensure infection control practices (proper hand hygiene, isolation if necessary) to prevent spread, especially in healthcare settings or childcare centers.

Strengthen preventive interventions: Improving access to clean water, sanitation, and hygiene (WASH) is fundamental to reducing the incidence of dysentery. Public health programs should continue to promote basic food safety and handwashing practices to curb the spread of Shigella, E. coli, and other pathogens    .

Vaccine development: There is an urgent need for effective vaccines against Shigella and EHEC. Given the disease burden, an affordable Shigella vaccine for children could significantly reduce morbidity and mortality. Current findings call for accelerated efforts in this area . Similarly, research into vaccines or passive immunoprophylaxis for EHEC (targeting Shiga toxin) should be supported to eventually prevent HUS.

Antimicrobial resistance surveillance: Global surveillance for antibiotic resistance patterns in enteric pathogens should be enhanced. Up-to-date local data on Shigella and Campylobacter resistance can inform empirical treatment guidelines. Investment in laboratory capacity in developing regions will aid this effort.

Diagnostic innovation: Development of low-cost, point-of-care diagnostic tests for the main dysentery pathogens would allow clinicians to distinguish causes rapidly and tailor treatment (for example, a rapid combo test that differentiates Shigella vs. STEC vs. E. histolytica). Research and funding towards such diagnostic tools could greatly improve case management in rural or resource-poor settings.

Clinical management research: Further clinical trials or operational research in areas such as optimal antibiotic duration for dysentery, the role of newer agents (e.g., rifaximin or other non-absorbed antibiotics for EHEC? or adjunctive therapies for HUS like eculizumab), and the impact of probiotics specifically in dysentery would help refine treatment protocols. Also, studies on managing dysentery in malnourished children (a particularly vulnerable group) can provide insights into nutritional supplementation or adjunct therapies required.

Long-term outcomes: Cohort studies following children who recovered from severe dysentery could elucidate long-term impacts (on growth, gut health, cognitive development). This would underscore the full benefits of preventing and aggressively treating these infections beyond the immediate survival.

By implementing these recommendations in clinical practice and pursuing the outlined research and public health initiatives, we can move toward the goal of minimizing the toll of acute hemocolitic infections in children. While significant progress has been made in the past few decades (e.g., widespread ORT use has saved millions of lives), dysentery remains a scourge in many low-resource settings and a persistent threat anywhere sanitation fails. A comprehensive, evidence-based approach – combining prompt treatment, preventive strategies, and innovation – is essential to protect children worldwide from this condition and its consequences.

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