**HUS Risk – Bloody Diarrhea v1.0**

**ED PHASE**

**Inclusion Criteria**
- Age >4 months (or eating solid foods) with bloody diarrhea OR non-bloody diarrhea and any HUS Risk Factors

**Exclusion Criteria**
- Patients with
  - known HUS
  - known or suspected malignancy
  - hemorrhagic shock
  - known inflammatory bowel disease (IBD)
  - known renal disease
  - concern for intussusception

**Initial Management**
- Visual rectal exam to exclude anatomic source of bleeding
- Stool PCR (rectal swab OK)
- Review outside labs, if available
- Obtain Labs (if outside labs not available):
  - CBC with diff.
  - BUN/creatinine
  - Urinalysis
  - Electrolytes
  - PIV placement
  - NS boluses as needed for poor perfusion or signs of dehydration. Most patients will require at least one NS bolus.

<table>
<thead>
<tr>
<th>Labs Concerning for HUS</th>
<th>Stool PCR positive for STEC</th>
<th>Stool PCR negative for STEC</th>
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</thead>
<tbody>
<tr>
<td>Any of the three criteria:</td>
<td></td>
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<tr>
<td>· Hemolytic anemia (Hgb&lt;10g/dL, positive schistocytes)</td>
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<tr>
<td>· Thrombocytopenia (platelet count &lt;150k)</td>
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<tr>
<td>· Acute kidney injury (elevated BUN/Cr)</td>
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<td>Or these trends:</td>
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<td>· &gt; 5% decrease in platelet count since onset of symptoms</td>
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<tr>
<td>· Rising BUN/creatinine since onset of symptoms</td>
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<tr>
<td><strong>Any labs concerning for HUS = Yes</strong></td>
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<tr>
<td>· Consult Nephrology</td>
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<tr>
<td>· Admit to Nephrology or Gen Med</td>
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<tr>
<td><strong>Go to Inpatient Phase</strong></td>
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<tr>
<td><strong>Labs Concerning for HUS = No</strong></td>
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<tr>
<td>· Discharge if patient does not meet Admit Criteria</td>
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<td></td>
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<tr>
<td>· Admit if patient meets Admit Criteria</td>
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<tr>
<td><strong>Consider alternate diagnosis (e.g. acute gastroenteritis, new diagnosis IBD, intussusception, Meckel’s diverticulum)</strong></td>
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<tr>
<td><strong>Off Pathway</strong></td>
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</tr>
</tbody>
</table>

**Patient Discharge Instructions**
- Encourage fluid intake
- Next day follow-up with PCP or Urgent Care/ED for labs
- Public Health: Seattle & King County STEC Information
- Return to ED if any of the following:
  - New bleeding, bruising, petechial rash
  - Severe abdominal pain
  - Unusual/severe headache
  - No urine output for 12 hours
  - Irritability
  - Edema

**Admit Criteria**
- ANY of the following:
  - Symptoms ≤ 4 days (or uncertain)
  - Ill-appearing
  - Unable to tolerate PO fluids
  - Use of antibiotics during illness
  - Any labs concerning for HUS
  - Unable to complete Follow-Up Plan (see below)

**Discharge with Follow-Up Plan**
- Follow up must be arranged for labs (CBC with diff. and BUN/creatinine) and hydration evaluation within 24hrs with PCP or Urgent Care/ED.
- Return to ED if labs concerning for HUS

**Admit to Gen Med**
- Evaluate patient’s perfusion to determine if additional NS boluses are needed
- If normal perfusion, initiate Maintenance IV Fluid Pathway
- Contact precautions

**HUS Risk Factors**
- Exam findings (petechial rash, edema, hypertension, pallor)
- Eating raw/undercooked meat
- Farm visits or farm animal contact
- Close contact with known Shiga Toxin E.Coli (STEC) infected person

**Hemolytic Uremic Syndrome**

**Public Health Contact**

**For questions concerning this pathway,**

**Seattle Children’s Hospital**

**Last Updated: January 2018**

**Next Expected Review: January 2023**

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### INPATIENT PHASE

**HUS Criteria (need all three)**
- Hemolytic anemia (Hgb<10g/dL, positive schistocytes)
- Thrombocytopenia (platelet <150k)
- Acute kidney injury (elevated BUN/creatinine)

**Exclusion Criteria**
- Patients with:
  - known HUS
  - known or suspected malignancy
  - hemorrhagic shock
  - known inflammatory bowel disease (IBD)
  - known renal disease
  - concern for intussusception

**Ongoing Management**
- Evaluate patient’s perfusion to determine if additional NS boluses are needed
- Initiate/continue Maintenance IV Fluid Pathway
- Monitor strict I/O, including daily weights
- Regular diet in addition to full maintenance fluids

**HUS Risk Factors**
- Exam findings (petechial rash, edema, hypertension, pallor)
- Eating raw/undercooked meat
- Farm visits or farm animal contact
- Close contact with known Shiga Toxin E.Coli (STEC) infected person

**Check Daily Labs**
- BUN/Creatinine
- CBC with diff
- Electrolytes

**Discharge Criteria**
- Two sets of normal labs that are at least 24 hours apart
- Eating well and well appearing
- No social/family concerns
- Reliable follow-up in 24-48 hours
- Outpatient plan accepted by PMD and family

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**Labs Concerning for Developing HUS**
- Any of the above HUS criteria
  - OR
  - > 5% decrease in platelet count since onset of symptoms
  - OR
  - Rising BUN/Creatinine since onset of symptoms

**HUS = Hemolytic Uremic Syndrome**

**Off Pathway**

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**Patient Discharge Instructions**
- Encourage fluid intake
- Follow up with PCP in 24-48 hours
- **Public Health – Seattle & King County STEC Information**
- Return to ED if any of the following:
  - New bleeding, bruising, petechial rash
  - Severe abdominal pain
  - Unusual/severe headache
  - No urine output for 12 hours
  - Irritability
  - Edema

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**HUS Risk – Bloody Diarrhea v1.0**

- Inclusion Criteria
  - Age >4 months (or eating solid foods) with bloody diarrhea OR non-bloody diarrhea and any HUS Risk Factors

- Exclusion Criteria
  - known HUS
  - known or suspected malignancy
  - hemorrhagic shock
  - known inflammatory bowel disease (IBD)
  - known renal disease
  - concern for intussusception

- **HUS Criteria**
- **HUS Risk Factors**
- **Inclusion Criteria**
- **Exclusion Criteria**
- **Patient Discharge Instructions**

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For questions concerning this pathway, contact: HUSRiskBloodyDiarrheaPathway@seattlechildrens.org

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Last Updated: January 2018
Next Expected Review: January 2023
HUS Risk – Bloody Diarrhea Pathway

Introduction

• This clinical standard work pathway is designed to aid in the prevention and diagnosis of hemolytic uremic syndrome (HUS) in children with bloody and non-bloody diarrhea.

• Over 1000 children present to the SCH ED with diarrhea each year

• About 10 are diagnosed there with HUS annually at SCH
Shiga-Toxic *E. coli* (STEC) Infection

- Any diarrheagenic Enterohemorrhagic *E. coli* (EHEC) infection that produces shigatoxin (also known as verotoxin) places a child at risk for HUS.
- EHEC infects human intestine where it produces shigatoxin and induces diarrhea.
- Synonyms include STEC (Shiga Toxin *E. coli*) and VTEC (Verotoxigenic *E. coli*).
- There are about 4000 cases of STEC annually in the US.
- Abdominal pain & watery diarrhea develop 3-7 days after ingestion of STEC.
- Usually (not always!) followed by bloody stool.
- Most patients with Hemolytic Uremic Syndrome (HUS) have associated STEC infection.
  - 10-15% of children with STEC develop HUS.
Shiga-Toxic *E. coli* (STEC) Infection

Keithlin 2014
When evaluating a patient with bloody diarrhea, consider the multiple possible differential diagnoses that may be more common than STEC enteritis.

Test and treat as clinically indicated.

Consider alternative diagnosis (e.g. acute gastroenteritis, new diagnosis IBD, intussusception, Meckel’s diverticulum).
Hemolytic Uremic Syndrome (HUS)

- All three criteria are required to diagnose HUS
- Supportive but non-diagnostic concomitant symptoms include: CNS (seizures, headache), GI (severe pain, rectal prolapse, intussusception), Cardiac (failure, ischemia), Pancreatic (pancreatitis) and Hematologic (DIC) manifestations

**HUS Criteria (need all three)**
- Hemolytic anemia (Hgb<10g/dL, positive schistocytes)
- Thrombocytopenia (platelet <150k)
- Acute kidney injury (elevated BUN/creatinine)

**HUS Risk Factors**
- Exam findings (petechial rash, edema, hypertension, pallor)
- Eating raw/undercooked meat
- Farm visits or farm animal contact
- Close contact with known Shiga Toxin E.Coli (STEC) infected person

**Labs Concerning for HUS**

Any of the three criteria:
- Hemolytic anemia (Hgb<10g/dL, positive schistocytes)
- Thrombocytopenia (platelet <150k)
- Acute kidney injury (elevated BUN/Cr)

Or these trends:
- > 5% decrease in platelet count since onset of symptoms
- Rising BUN/Creatinine since onset of symptoms
Rapid Stool PCR

• Traditional Stool Culture
  • $411 (inpatient), $350 (outpatient) minimum
  • Potentially SEVERAL HUNDRED DOLLARS MORE than PCR, depending on pathogen/susceptibility testing

• New Rapid PCR
  • $600 (inpatient), $575 (outpatient)
  • Reflexive culture for ‘cultivable’ pathogens

1 Test. 22 Targets. All in about an hour.

**Bacteria**
- Campylobacter (jejuni, coli and upsaliensis)
- Clostridium difficile (toxin A/B)
- Plesiomonas shigelloides
- Salmonella
- Yersinia enterocolitica
- Vibrio (parahaemolyticus, vulnificus and cholerae)
  - Vibrio cholerae
- Diarrheagenic E. coli/Shigella
  - Enteropathogenic E. coli (EPEC)
  - Enteroaggregative E. coli (EAEC)
  - Enterotoxigenic E. coli (ETEC) lt/st
  - Shiga-like toxin-producing E. coli (STEC) stx1/stx2
  - E. coli 0157
  - Shigella/Enteroinvasive E. coli (EIEC)

**Parasites**
- Cryptosporidium
- Cyclospora cayetanensis
- Entamoeba histolytica
- Giardia lamblia

**Viruses**
- Adenovirus F 40/41
- Astrovirus
- Norovirus GI/GII
- Rotavirus A
- Sapovirus (I, II, IV and V)
Rapid Stool PCR

- Consider referencing 2017 Infectious Diseases Society of America Clinical Practice Guidelines for the Diagnosis and Management of Infectious Diarrhea

- If negative for STEC but positive for other pathogen, treat as indicated

- Return to ED
- Return to Inpatient
Initial Management

- Initial Labs to assess for signs of HUS
- Early urinalysis may show renal involvement or suggest alternate diagnosis
- CBC to look for hemolysis/thrombocytopenia
- Electrolytes to help assess for renal involvement/dehydration
- Stool PCR (rapid, accurate, cost-effective)
Laboratory Studies (expanded)

**Additional Labs**
Order the following with the first set of daily labs:
- Bilirubin
- Coags
- Direct Antibody Test (Coombs)
- Haptoglobin
- LDH

- Should be obtained during hospitalization
- May aid in the diagnosis of early HUS or help risk-stratify in the event of HUS development
IV Fluids

- NS boluses as needed for poor perfusion or signs of dehydration. Most patients will require at least one NS bolus.

![Use caution with IV fluids in patients with abnormal GFR]

- One systematic review has shown that patients who receive IV fluids in the first 4 days of STEC infection develop less severe HUS
  - No evidence of harm from appropriate use of IV fluids after 4 days of symptoms
  - Non-randomized trials have also shown that IV fluids may potentially prevent HUS altogether in patients at increased risk

Grisaru 2017
There is known benefit in patients that develop HUS to receiving IV fluids within the FIRST FOUR DAYS of diarrhea onset.

In the absence of evidence of harm, we recommend admission for IV fluids in the FIRST ONE WEEK of diarrhea onset.

Grisaru 2017
Patient Discharge Instructions

- Encourage fluid intake
- Next day follow-up with PCP or Urgent Care/ED for labs
- Public Health Infection Prevention
- Return to ED if any of the following:
  - New bleeding, bruising, petechial rash
  - Severe abdominal pain
  - Unusual/severe headache
  - No urine output for 12 hours
  - Irritability
  - Edema
Discharge Criteria/Instructions (Inpatient)

**Discharge Criteria**
- Two sets of normal labs that are at least 24 hours apart
- Eating well and well appearing
- No social/family concerns
- Reliable follow-up in 24-48 hours
- Outpatient plan accepted by PMD and family

**Patient Discharge Instructions**
- Encourage fluid intake
- Follow up with PCP in 24-48 hours
- Public Health – Seattle & King County
- STEC Information
- Return to ED if any of the following:
  - New bleeding, bruising, petechial rash
  - Severe abdominal pain
  - Unusual/severe headache
  - No urine output for 12 hours
  - Irritability
  - Edema

• In the absence of convincing evidence, the recommendation for two sets of normal labs at least 24 hours apart is based on local and national expert consensus
1. Hemolytic Uremic Syndrome (HUS) is diagnosed by which of the following laboratory abnormalities:
   a. hemoglobin <10g/dL or positive schistocytes seen on peripheral smear
   b. platelet count <150k
   c. elevated BUN/creatinine for age
   d. all of the above

2. One systematic review has shown that patients who receive IV fluids in the first four days of STEC infection develop MORE severe HUS. True or False.
   a. True
   b. False

3. A patient with bloody diarrhea for 10 days who is well-appearing, tolerating PO fluids, with no labs concerning for HUS, can be discharged home from the ED if reliable follow-up can be arranged within 24 hours. True or False.
   a. True
   b. False
HUS Risk – Bloody Diarrhea Approval & Citation

Approved by the CSW HUS Risk - Bloody Diarrhea team for January 10, 2018

CSW Bloody Diarrhea Team:

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Infectious Disease, Stakeholder: Matthew Kronman, MD, MSCE
Pathology, Stakeholder: Xuan Qin, PhD
Nephrology, Stakeholder: Jordan Symons, MD
Hospital Medicine, Stakeholder: Suzanne Sundermann, MD
Graduate Medical Education, Stakeholder: Carson Burns, MD

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CIS Informatician: Carlos Villavicencio, MD, MS/MI
CIS Analyst: Maria Jerome
Librarian: Sue Groshong, MLIS
Program Coordinator: Kristyn Simmons

Executive Approval:

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Sr. VP, Chief Nursing Officer: Madlyn Murrey, RN, MN
Surgeon-in-Chief: Bob Sawin, MD

Retrieval Website: http://www.seattlechildrens.org/pdf/HUS-Risk-Bloody-Diarrhea-Pathway.pdf

Please cite as:
Evidence Ratings

This pathway was developed through local consensus based on published evidence and expert opinion as part of Clinical Standard Work at Seattle Children’s. Pathway teams include representatives from Medical, Subspecialty, and/or Surgical Services, Nursing, Pharmacy, Clinical Effectiveness, and other services as appropriate.

When possible, we used the GRADE method of rating evidence quality. Evidence is first assessed as to whether it is from randomized trial or cohort studies. The rating is then adjusted in the following manner (from: Guyatt G et al. J Clin Epidemiol. 2011;4:383-94.):

Quality ratings are *downgraded* if studies:
- Have serious limitations
- Have inconsistent results
- If evidence does not directly address clinical questions
- If estimates are imprecise OR
- If it is felt that there is substantial publication bias

Quality ratings are *upgraded* if it is felt that:
- The effect size is large
- If studies are designed in a way that confounding would likely underreport the magnitude of the effect OR
- If a dose-response gradient is evident

Guideline – Recommendation is from a published guideline that used methodology deemed acceptable by the team.

Expert Opinion – Our expert opinion is based on available evidence that does not meet GRADE criteria (for example, case-control studies).

**Quality of Evidence:**
- ⭐⭐⭐⭐ High quality
- ⭐⭐⭐ Moderate quality
- ⭐⭐ Low quality
- ⭐ Low quality

Guideline
Expert Opinion
Summary of Version Changes

- **Version 1.0 (01/10/2018):** Go live
Medical Disclaimer

Medicine is an ever-changing science. As new research and clinical experience broaden our knowledge, changes in treatment and drug therapy are required.

The authors have checked with sources believed to be reliable in their efforts to provide information that is complete and generally in accord with the standards accepted at the time of publication.

However, in view of the possibility of human error or changes in medical sciences, neither the authors nor Seattle Children’s Healthcare System nor any other party who has been involved in the preparation or publication of this work warrants that the information contained herein is in every respect accurate or complete, and they are not responsible for any errors or omissions or for the results obtained from the use of such information.

Readers should confirm the information contained herein with other sources and are encouraged to consult with their health care provider before making any health care decision.
Studies were identified by searching electronic databases using search strategies developed and executed by a medical librarian, Susan Groshong. Searches were performed in August, 2017, in the following databases – on the Ovid platform: Medline and Cochrane Database of Systematic Reviews; elsewhere: Embase, National Guideline Clearinghouse, TRIP and Cincinnati Children’s Evidence-Based Recommendations. In Medline and Embase, appropriate Medical Subject Headings (MeSH) and Emtree headings were used respectively, along with text words, and the search strategy was adapted for other databases using text words. Concepts searched were bloody diarrhea, hemolytic uremic syndrome, Escherichia coli infections, Shiga-toxigenic Escherichia coli and Shiga toxins. Retrieval was limited to 2007 to current, humans, English language and to certain evidence categories, such as relevant publication types, index terms for study types and other similar limits. Additional articles were identified by team members and added to results.

Susan Groshong, MLIS
August 16, 2017

Identification

- 330 records identified through database searching
- 23 additional records identified through other sources

Screening

- 351 records after duplicates removed

- 351 records screened
- 340 records excluded

Eligibility

- 11 records assessed for eligibility
- 6 full-text articles excluded,
  2 did not answer clinical question
  4 did not meet quality threshold

Included

- 5 studies included in pathway

Flow diagram adapted from Moher D et al. BMJ 2009;339:bmj.b2535


