

## MANAGEMENT OF CHILDREN WITH SPLENIC DYSFUNCTION

### Maine Medical Center / Barbara Bush Children's Hospital

#### GOALS:

1. To outline the diagnostic workup for suspected splenic dysfunction in pediatric patients.
2. To outline the empiric management of fever in pediatric patients with asplenia or splenic dysfunction.
3. To outline the antimicrobial prophylaxis in pediatric patients with asplenia or splenic dysfunction.
4. To outline the immunization recommendations for pediatric patients with splenic dysfunction and/or asplenia, including pre- and post-splenectomy.
5. To describe the indications for surgical splenectomy.

#### Background

The spleen is an organ of the reticuloendothelial system that functions as a filter for blood cells and opsonized pathogens and trigger for innate and adaptive immune responses to pathogens. The spleen plays a critical role in defense against infection. Asplenia/hyposplenia are associated with increased morbidity and mortality from complications of infection.<sup>1</sup> The incidence of sepsis post-splenectomy in children is ~1.8 to 3 per 100 person-years, with children <3 years having the highest risk for infection.<sup>2</sup> The incidence of sepsis is substantially higher in the first 1 to 3 years post-splenectomy, though infections may occur as late as 50 years after the procedure.<sup>2-4</sup> Infections in patients with compromised splenic function are most commonly due to encapsulated bacteria (e.g. pneumococcal, meningococcal, *Hemophilus influenzae* type B).<sup>5</sup> Given its role in erythrocyte clearance, intraerythrocytic parasitic infections (e.g. *Babesia*, malaria) may be seen.<sup>6-8</sup> Patients with decreased splenic function are difficult to identify, and routine, easily applicable, standardized methods for diagnosis of functional asplenia/hyposplenia are not well described.<sup>9, 10</sup>

#### Definitions

- A. Asplenia/hyposplenia are defined as absent/diminished spleen function
- B. Causes of asplenia/hyposplenia include (Table 1):
  1. Congenital
  2. Surgical
  3. Functional

#### Diagnostic workup for suspected asplenia/hyposplenia

- A. Potential methods of evaluating splenic function are based on derangements in the two primary functions of the spleen, phagocytic and immunologic, and include hematologic tests and scintigraphy (Table 2)
- B. Patients who have undergone splenectomy or have medical conditions known to confer a major risk of hyposplenism do not require additional workup for assessment of splenic function<sup>9</sup>
- C. Patients with medical conditions predisposing to hyposplenism, but not known to confer a major risk of hyposplenism, may undergo evaluation of splenic function using any of the methods described in Table 2
- D. Patients with heterotaxy should follow recommendations as outlined in figure 1.

#### Management of fever in the patient with asplenia/hyposplenia

- A. Fever is defined as temperature greater than or equal to 38.3 C (101 F)
- B. Initial laboratory evaluation of a patient with known or suspected asplenia/hyposplenia should include:
  1. CBCD
  2. CMP
  3. Blood culture
    - i. If a central line is present, a blood culture should be drawn from each lumen of the central line

- ii. If no central line is present, a single peripheral blood culture should be drawn
  - iii. Collect per institutional guidelines.
- C. Additional evaluations may be considered if clinically indicated based on history and exam
  - 1. Urinalysis and urine culture
  - 2. Viral testing (e.g. COVID-19, influenza, RSV)
  - 3. CXR
  - 4. Other
- D. Empiric antibiotic therapy
  - 1. Ceftriaxone (50 mg/kg q24 hours; max dose 2 g)
  - 2. In the case of cephalosporin allergy: Levofloxacin 10 mg/kg q24 hours if  $\geq 5$  years (max dose 750 mg) or 10 mg/kg/dose q12 hours if  $< 5$  years
- E. Indications for admission
  - 1. Unwell appearance
  - 2. Severe sepsis, defined as one of the following organ system effects
    - i. Cardiovascular (if despite boluses totaling  $\geq 40$  mL/kg (typical bolus is 20 mL/kg over 1 hour)
      - 1. Hypotension  $< 5^{\text{th}}$  percentile
      - 2. Vasoactive medications at any dose
      - 3.  $\geq 2$  of the following:
        - a. Capillary refill  $> 5$  seconds
        - b. Core to peripheral temperature gap  $> 3^{\circ}\text{C}$
        - c. Urine output  $< 0.5$  mL/kg/hr
        - d. Unexplained metabolic acidosis (base deficit  $> 5.0$  mEq/L)
        - e. Blood lactate  $> 2 \times \text{ULN}$
    - ii. Respiratory
      - 1. ARDS *or*
      - 2. Intubated *or*
      - 3.  $> 50\%$  FiO<sub>2</sub> to keep SaO<sub>2</sub>  $> 92\%$
    - iii. Neurologic
      - 1. GCS  $\leq 11$  *or*
      - 2. Acute decline in GCS  $\geq 3$  from abnormal baseline
    - iv. Renal
      - 1. Creatinine  $\geq 2 \times \text{ULN}$  for age *or*
      - 2. 2-fold increase in baseline
    - v. Hepatic
      - 1. Bilirubin  $\geq 4$  mg/dL *or*
      - 2. ALT  $\geq 2 \times \text{ULN}$  for age
  - 3. History of bacteremia
  - 4. Social complexities
- F. Discharge criteria
  - 1. Clinically improved and with no comorbidity that requires hospitalization
  - 2. No clearly defined bacterial infection (e.g. culture negative and/or no localized infection)
  - 3. Afebrile for 24 hours prior to discharge

### **Antibiotic prophylaxis for patients with asplenia/hyposplenia**

- A. Daily antibiotic prophylaxis is recommended for children with asplenia, regardless of their immunization status, for the prevention of pneumococcal disease on the basis of trials that demonstrated a reduction in pneumococcal infection among children with sickle cell disease receiving penicillin prophylaxis.<sup>11-13</sup>

Patients with known or suspected hyposplenism should follow the same recommendations. Patients with heterotaxy should follow recommendations as outlined in figure 1.

- B. Routine antibiotic prophylaxis therapy
  - 1. Children < 3 years: oral penicillin V 125 mg twice daily<sup>11, 12</sup> (alternative in the case of allergy: erythromycin 125 mg BID).<sup>11</sup>
  - 2. Children ≥ 3 years: oral penicillin V 250 mg twice daily<sup>11, 12</sup> (alternative in the case of allergy: erythromycin 250 mg BID).<sup>11</sup>
- C. Duration of routine antibiotic prophylaxis
  - 1. There is little consensus on the duration, with recommendations based on patient age, time since splenectomy, prior episode of bacteremia, and degree of immunocompromise
  - 2. Lifelong prophylaxis is recommended for the following populations:<sup>12</sup>
    - i. Previous episode of pneumococcal bacteremia or other invasive pneumococcal disease
    - ii. Immunocompromised state for reason(s) other than asplenia/hyposplenia
  - 3. United States and Australian recommendations are to continue antibiotic prophylaxis for 1-3 years post-splenectomy and until > 5 years<sup>12</sup>
  - 4. United Kingdom recommendations are to continue antibiotic prophylaxis until > 16 years and indefinitely in patients with inadequate serologic response to pneumococcal vaccination<sup>9</sup>
  - 5. We recommend continuing antibiotic prophylaxis for 1 year post-splenectomy or until 5 years of age, whichever is later, unless any of the conditions in C.2. are met.

### **Immunizations for patients with asplenia/hyposplenia**

- A. In addition to routine vaccines, the following vaccines are recommended for patients with asplenia/hyposplenia:
  - 1. Pneumococcal
  - 2. Meningococcal
  - 3. *H. influenza* type b (Hib)
  - 4. Influenza
- B. Vaccination should be completed at least 2 weeks before planned splenectomy
- C. Recommend an ID referral/consult at least 1 month prior to planned splenectomy
- D. If vaccinations are not able to be completed before splenectomy, administration should be initiated ~2 weeks after splenectomy<sup>12</sup>
- E. If there are any anticipated social/geographic barriers in returning for follow-up care following splenectomy, consideration should be made to giving vaccinations prior to discharge
- F. Refer to the CDC website for the most updated vaccine guidelines regarding pneumococcal, meningococcal and Hib vaccinations: [www.cdc.gov/vaccines/schedules](http://www.cdc.gov/vaccines/schedules)
- G. Influenza vaccination<sup>12</sup>
  - 1. Annual vaccination of patient and eligible household members is recommended
  - 2. Patient should receive an inactivated vaccine
- H. Consider referral to pediatric ID for animal bites, travel or other more nuanced situations

### **Indications for surgical splenectomy**

- A. Hereditary spherocytosis
  - 1. Most common hematologic abnormality requiring surgical treatment
  - 2. Indication(s) to operate:
    - i. Decision must weigh severity of disease, age, risk of procedure
    - ii. No current United States guidelines
    - iii. European guidelines recommend splenectomy for patients who are transfusion-dependent or suffer severe anemia,<sup>14</sup> defined as hemoglobin 6-8 g/dL, reticulocyte

count > 10%, and bilirubin > 3 mg/dL,<sup>15</sup> and ideally after 6 years old to avoid the younger, higher-risk period of asplenia<sup>14</sup>

3. Perioperative consideration(s): none
  4. Technique: total versus partial splenectomy is controversial;<sup>16-19</sup> shared decision-making between surgery, hematology, and parents is necessary
- B. Sickle cell disease
1. Indication(s) to operate:
    - i. Splenic sequestration
    - ii. Single or multiple vaso-occlusive crises is controversial
  2. Perioperative consideration(s): maintain hydration and hemoglobin; avoid pain
  3. Technique: total splenectomy
- C. Immune thrombocytopenic purpura (ITP)
1. Indication(s) to operate: failure of medical management, life-threatening bleeding
  2. Perioperative consideration(s):
    - i. Pre-operative platelet count should ideally be > 50K but may not be achievable
    - ii. Consider IVIG within 1 week of surgery or platelet infusion during surgery until the artery is divided
  3. Technique: total splenectomy
- D. Splenic trauma
1. Indication(s) to operate: persistent hemodynamic instability despite blood transfusion based on ATOMAC pediatric trauma consortium guidelines
  2. Perioperative consideration(s): none
  3. Technique: total versus partial splenectomy; attempt to salvage some or all of the spleen if possible
- E. Solid splenic mass
1. Most common are lymphoma and angiosarcoma
  2. Indication(s) to operate: diagnosis and/or treatment
  3. Perioperative consideration(s): none
  4. Technique: partial splenectomy if possible
- F. Splenic abscess
1. Indication(s) to operate: failure of medical management
  2. Perioperative consideration(s): none
  3. Technique: partial splenectomy if possible
- G. Splenic cysts
1. Most common anatomic abnormality requiring surgical treatment
  2. Indication(s) to operate: symptomatic or > 5 cm
  3. Perioperative consideration(s): none
  4. Technique: partial splenectomy if possible; unroofing and marsupialization have high recurrence rates
- H. Echinococcal cyst
1. Indication(s) to operate: primary therapy
  2. Perioperative consideration(s): none
  3. Technique: PAIR (puncture, aspiration, injection, re-aspiration). Splenectomy only for abscess or hemorrhage
- I. Wandering spleen
1. Indication(s) to operate: primary therapy
  2. Perioperative consideration(s): none
  3. Technique: immobilization with extra peritoneal pocket or mesh basket or omental sling
- J. General postoperative consideration(s): consider antiplatelet therapy for platelets > 1 million

**Table 1:** Causes of asplenia/hyposplenia<sup>5, 20</sup>

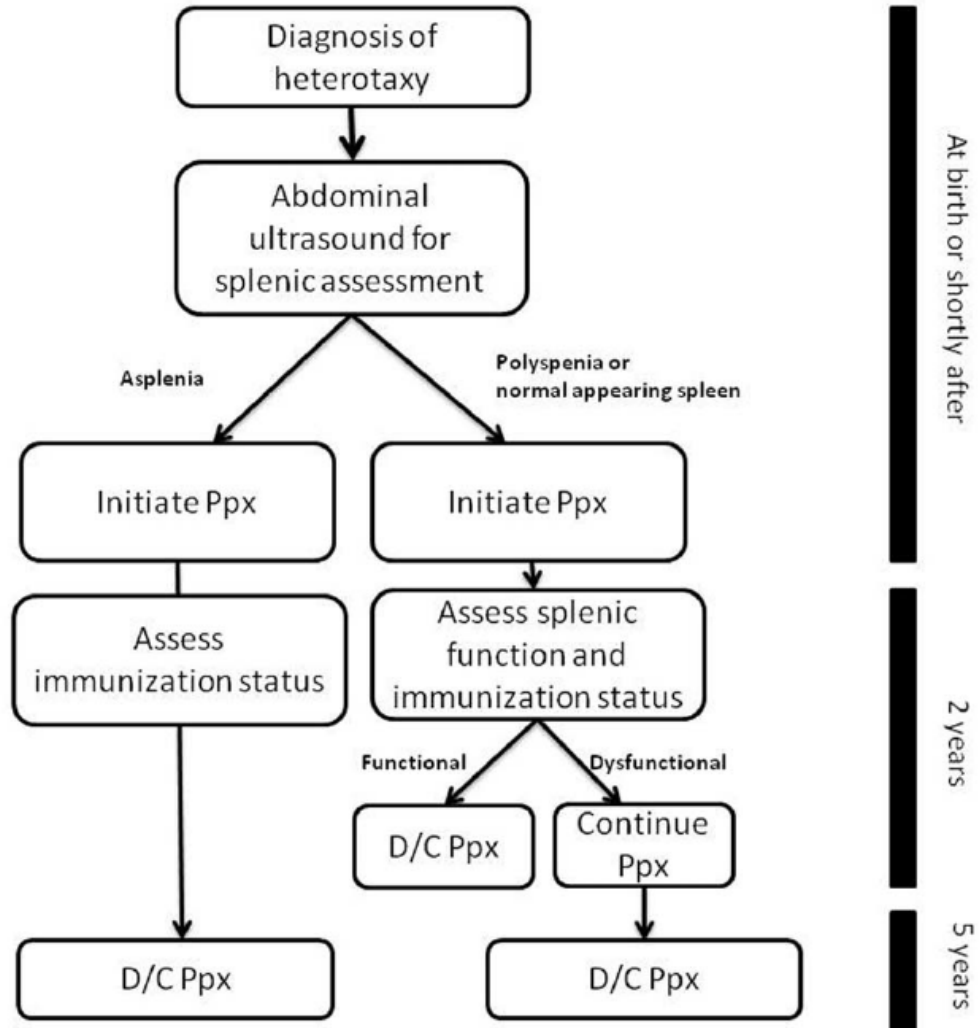
\*conditions known to confer hyposplenism or a major risk of hyposplenism

<b>Congenital*</b>	<b>Surgical*</b>
<ul style="list-style-type: none"> <li>- Isolated congenital asplenia</li> <li>- Heterotaxy syndromes (e.g. Ivemark syndrome)</li> <li>- Congenital heart disease with laterally component</li> </ul>	<ul style="list-style-type: none"> <li>- Trauma</li> <li>- Splenic cyst, mass, abscess</li> <li>- Hemolytic disorders               <ul style="list-style-type: none"> <li>o Hereditary spherocytosis</li> <li>o Autoimmune hemolytic anemia</li> <li>o Immune thrombocytopenia</li> </ul> </li> <li>- Hypersplenism               <ul style="list-style-type: none"> <li>o Splenic sequestration</li> <li>o Gaucher’s disease</li> </ul> </li> </ul>
<b>Functional</b>	
<ul style="list-style-type: none"> <li>- Hematologic conditions               <ul style="list-style-type: none"> <li>o Sickle cell disease*</li> <li>o Thalassemia</li> <li>o Other hemoglobinopathies</li> <li>o Histiocytosis</li> <li>o Fanconi’s anemia</li> </ul> </li> <li>- Neoplastic conditions               <ul style="list-style-type: none"> <li>o Chronic grave-versus-host disease after allogenic hematopoietic stem cell transplant</li> </ul> </li> <li>- Gastrointestinal conditions               <ul style="list-style-type: none"> <li>o Celiac disease</li> <li>o Ulcerative colitis</li> <li>o Intestinal lymphangiectasia</li> <li>o Whipple’s disease</li> <li>o Cirrhosis</li> <li>o Chronic active hepatitis</li> </ul> </li> <li>- Vascular conditions               <ul style="list-style-type: none"> <li>o Splenic artery occlusion</li> <li>o Splenic vein occlusion</li> <li>o Celiac artery occlusion</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>- Autoimmune conditions               <ul style="list-style-type: none"> <li>o Vasculitis (splenic infarction)</li> <li>o Systemic lupus erythematosus</li> <li>o Antiphospholipid syndrome</li> <li>o Rheumatoid arthritis</li> <li>o Grave’s disease</li> <li>o Sjögren’s syndrome</li> <li>o Polyarteritis nodosa</li> </ul> </li> <li>- Infectious conditions               <ul style="list-style-type: none"> <li>o HIV</li> </ul> </li> <li>- Infiltrative conditions               <ul style="list-style-type: none"> <li>o Storage disease (e.g. Gaucher’s disease)</li> <li>o Amyloidosis with splenic involvement</li> <li>o Sarcoidosis with splenic involvement</li> </ul> </li> <li>- Other conditions               <ul style="list-style-type: none"> <li>o Splenic irradiation</li> <li>o Total parenteral nutrition</li> <li>o High-dose corticosteroid therapy</li> </ul> </li> </ul>

**Table 2:** Diagnostic techniques for evaluation of functional asplenia/hyposplenia<sup>10, 21-24</sup>

<b>Study</b>	<b>Description</b>	<b>Advantage(s)</b>	<b>Disadvantage(s)</b>
Howell-Jolly body (HJB) detection	Nuclear remnants found in erythrocytes	Simple, no need for special equipment	Not as sensitive for mild splenic hypofunction
Pitted red blood cell detection	Erythrocyte membrane irregularities (pit count > 4% has been associated with hyposplenism)	More sensitive than HJB detection	Requires specialized microscopy
<sup>99m</sup> Techneium-labeled sulfur-colloid spleen scan	Quantification of splenic uptake of the radioisotope. Preferable for patients with known anatomy	Easier to perform and lower radioisotope dose than <sup>99m</sup> Techneium-labeled heat-damaged red blood cell scan	Radioisotope is taken up by phagocytes of the reticuloendothelial system. Splenic uptake may be masked by liver uptake, which may be problematic in the setting of heterotaxy
<sup>99m</sup> Techneium-labeled heat-damaged red blood cell scan	Quantification of splenic uptake of the radioisotope. Preferable for patients without known anatomy. Most useful to detect small amounts of splenic tissue or confirm or exclude defects seen on radiocolloid study	Radioisotope is preferentially taken up by the spleen, and thus more specific in the setting of heterotaxy	More time intensive and higher radioisotope dose than <sup>99m</sup> Techneium-labeled sulfur-colloid spleen scan

**Figure 1:** Algorithm for evaluation of splenic function and antibiotic prophylaxis in patients with heterotaxy (Loomba et al. Congenit Heart Dis. 2016)



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