Infections in Asplenic Patients

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Kurt Myers, MD, MBA
Assistant Professor
Division of Hospital Medicine
University of Kentucky College of Medicine

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Learning Objectives

Review . . .

- Basic splenic anatomy
- Types, causes & consequences of asplenia / hyposplenism
- Microorganisms associated w/ overwhelming infection in asplenic patients
- Management of fever & sepsis in asplenic patients
- Recommended vaccinations in asplenic patients

Spleen

Spleen

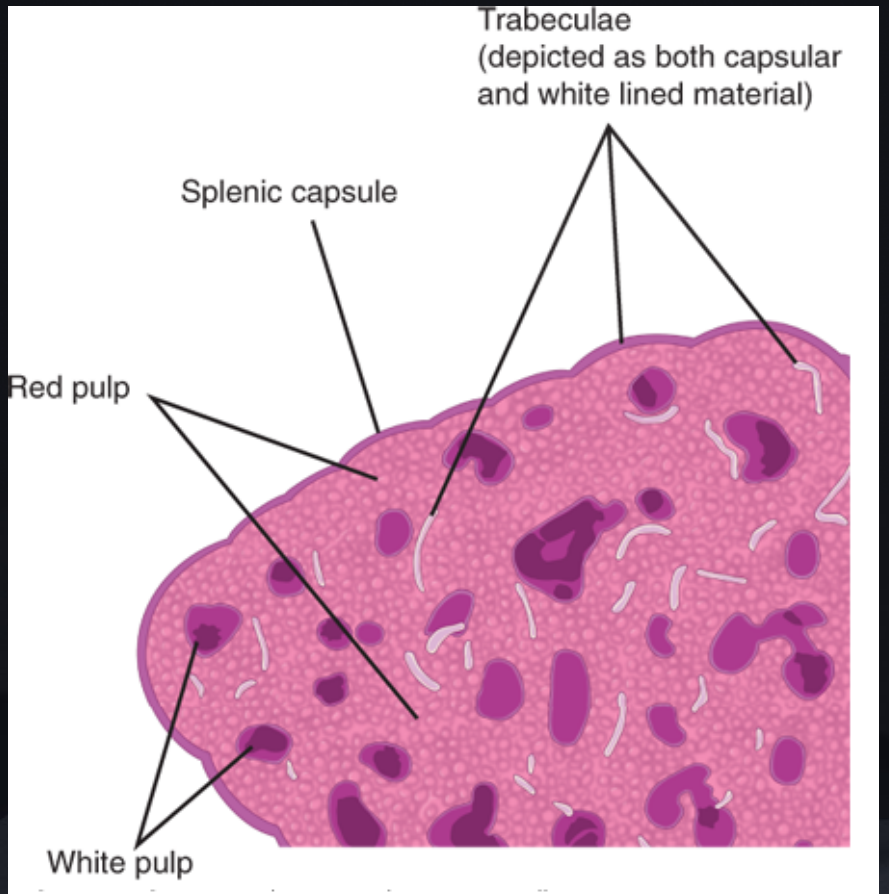
Basics

- Located in LUQ lateral to pancreatic tail & stomach
- About size of fist
- Accounts for ~25% of total lymphoid mass
- Contains ~50% of monocytes & Ig-producing B-cells
- Non-essential organ

Spleen

Anatomy

- Encased in connective tissue capsule
- Consists of 3 zones
  - (1) Red pulp
  - (2) White pulp
  - (3) Marginal zone



Source: F.C. Brunicardi, D.K. Andersen, T.R. Billiar, D.L. Dunn, L.S. Kao, J.G. Hunter, J.B. Matthews, R.E. Pollock: Schwartz's Principles of Surgery, 11e

Red Pulp

Filtration & phagocytosis

- Composed of . . .
  (1) Sinusoids (ie, wide blood vessels)
  (2) Connective tissue cords (Cord of Bilroth)
- Filters old/damaged RBCs
- Contains macrophages that phagocytose microorganisms (ie, viruses, bacteria, fungi)
- Reservoir for WBCs & platelets prior to release for inflammation/wound healing

White Pulp

Antibody synthesis

- Surrounded by red pulp
- Composed of . . .
  (1) Periarteriolar lymphoid sheath (PALS)
  (2) Lymphatic nodules
- Involved w/ initiation of adaptive immune response
- Produces & matures lymphocytes for Ab/Ig production

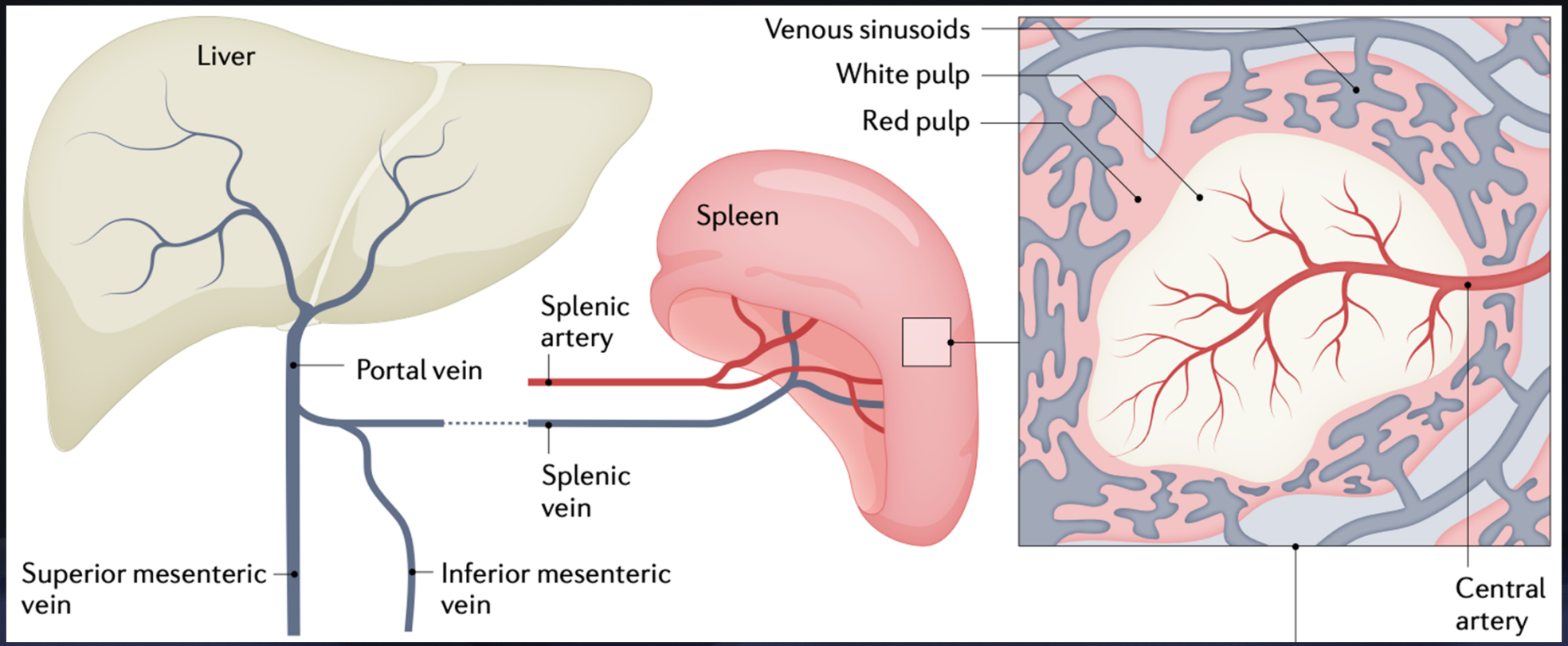
Marginal Zone

- Separates red pulp & white pulp
- Contains T-cells
- Filters pathogens out of blood into white pulp

Spleen

Vascular Supply & Drainage

- Arterial supply from **splenic artery** from celiac trunk
  - Splenic artery divides into 5 branches (do not anastomose)
- Veinous drainage via **splenic vein**
  - Run posterior to pancreas
  - Joins superior mesenteric vein form portal vein


Liver
Portal vein
Splenic artery
Splenic vein
Spleen
Superior mesenteric vein
Inferior mesenteric vein
Venous sinusoids
White pulp
Red pulp
Central artery

Spleen

Innervation / Nervous Supply

- **Sympathetic** innervation from **splenic nerve via celiac plexus**
  - **Reduces** inflammatory response

- **Parasympathetic** innervation from **vagus nerve (CN X)**
  - **Stimulates** inflammatory response

Asplenia

Asplenia

Basics

- DEF - Absence of spleen
- Types

  (1) **Anatomic** asplenia - Literal absence of spleen

  (2) **Functional** asplenia - Spleen present but does NOT function

Epidemiology

- Approximately 1 million asplenic patients in US
- About 25K splenectomies performed annually in US
- 70-100K of asplenic patients have sick cell anemia

Anatomic Aplsenia

- Types:
  1) Congenital
  2) Surgical (ie, due to splenectomy)

Congenital Asplenia

Rare

- Often associated w/ other congenital abnormalities
- **Ivemark Syndrome** - Type of heterotaxy syndrome
  - Congenital asplenia
  - Congenital heart disease
  - Abnormal anatomic position of other thoracic/abdominal internal organs

Surgical Asplenia

- Absence of spleen 2/2 **splenectomy**
- Splenectomy most commonly indicated 2/2 splenic trauma
- Spleen most commonly injured organ from blunt abdominal trauma

Surgical Asplenia

- Splenectomy also performed to manage splenomegaly & functional asplenia/hyposplenism 2/2 other disorders such as . . .
  - Lymphoma, leukemia, ITP
  - Hereditary spherocytosis, sickle cell anemia, thalassemia
  - EBV, HIV/AIDS, bacterial sepsis, malaria, schistosomiasis
  - Cirrhosis, venous obstruction, amyloidosis

Functional Asplenia / Hyposplenism

Functional Asplenia / Hyposplenism

- Spleen still anatomically present but . . .
  - Does not function at all (functional asplenia)

    . . . OR . . .

  - Does not function properly/effectively (hyposplenism)
- Seen w/ several diseases . . .
  - e.g, sickle cell anemia, GVH disease, celiac disease, alcoholic liver disease, IBD

TABLE 311.1 Medical Conditions Associated With Functional Hyposplenism

MEDICAL CONDITION	PREVALENCE OF HYPOSPLENISM	DEGREE OF HYPOSPLENISM	STRENGTH OF EVIDENCE FOR RISK OF SEPSIS
Sickle cell anemia	100%	Severe	+++
Graft-versus-host disease	15%–40%	Moderate to severe	+++
Celiac disease	33%–76%	Moderate to severe	+++
Human immunodeficiency virus–acquired immunodeficiency syndrome	36%	Moderate to severe	+++
Alcoholic liver disease	37%–100%	Moderate to severe	+++
Inflammatory bowel disease			++
Ulcerative colitis	35%–45%	Moderate	
Crohn disease	9%–37%	Mild	
Primary amyloidosis	28%	Moderate	++
Systemic lupus erythematosus	5%–7%	Mild to moderate	++

++, Moderate evidence; *+++*, strong evidence.
Modified from Di Sabatino A, Carsetti R, Corazza GR. Post-splenectomy and hyposplenic states. Lancet. *2011;378:86–97.*

- Hashimoto thyroiditis (ie, chronic lymphocytic/autoimmune thyroiditis)
- Rheumatoid arthritis
- Autoimmune polyglandular syndrome 1
- Multiple sclerosis
- Nephrotic syndrome
- High-dose corticosteroids
- Splenic irradiation
- Total parental nutrition
- Primary biliary cirrhosis
- Primary pulmonary hypertension
- NOTE: Hyposplenia can be reversible (ie, better control of underlying disease, less hyposplenism)

Immunologic Consequence of Asplenia / Hyposplenism

Impaired Immunologic Function

Basic pathophysiologic steps

(1) Decreased IgM & IgG production

(2) Decreased complement activation

(3) Decreased opsonization (specifically w/ C3b)

(4) Decreased phagocytosis of encapsulated bacteria

TABLE 311.2 Immunologic Defects After Splenectomy

DEFECT	MECHANISM
Decreased clearance of unopsonized bacteria	Depleted red pulp macrophages
Decreased clearance of cell-associated antibodies	Depleted red pulp macrophages
Decreased clearance of erythrocytes harboring malarial or babesial parasites	Depleted red pulp macrophages
Decreased processing of carbohydrate antigens	Depleted marginal zone macrophages
Decreased B-cell activation	Depleted marginal zone T cells
Decreased IgG2 and IgM antibodies	Depleted B cells in the germinal centers
Decreased CXC-chemokine ligand 12	Depleted CXC-chemokine receptor 4
Increased tumor necrosis factor	Depleted splenic nicotinic acetylcholine–producing T cells
Decreased recognition of pathogen-associated molecular patterns	Decreased Toll-like receptor networks in marginal zone macrophages
Decreased macrophage scavenger function	Decreased macrophage receptor with collagenous structure in marginal zone macrophages

CXC, Cysteine-X-cysteine (motif); *IgG2,* immunoglobulin G2; *IgM,* immunoglobulin M.

Evaluation of Splenic Function

- Peripheral smear
- Nuclear medicine (technetium-99m) liver/spleen scan

Peripheral Blood Smear

- Assess for presence of cellular or intracellular bodies typically filtered by spleen

  (1) Howell-Jolly bodies (cytoplasmic basophilic DNA remnants of RBC precursors)

  (2) Pappenheimer bodies (abnormal iron granules)

  (3) Pitted/Pocked RBCs

RBCs Findings w/ Asplenia/Hyposplenism

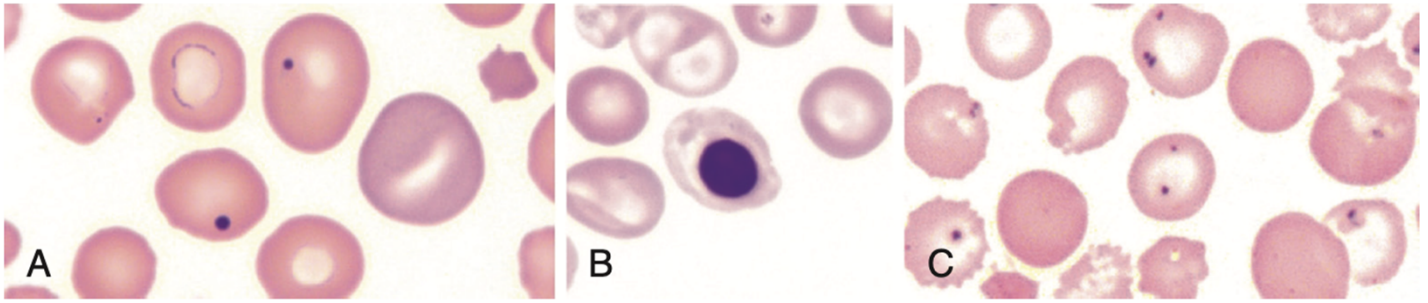


FIG. 311.2 Red cell findings in hyposplenism. (A) Red blood cells with Howell-Jolly bodies, which are cytoplasmic inclusions composed of nuclear remnants, as seen in patients with hyposplenism. (B) Nucleated red blood cell that occurs during red cell maturation but is typically cleared by a normal spleen. (C) Red blood cells with Pappenheimer bodies, which are siderotic granules that are irregular in shape and frequently multiple within a cell. *(From Connell NT, Shurin SB, Schiffman FJ. The spleen and its disorders. In: Hoffman R, Benz EJ Sr, Silberstein LE, eds.* Hematology: Basic Principles and Practice. *6th ed. Philadelphia: Saunders; 2012:2259.)*

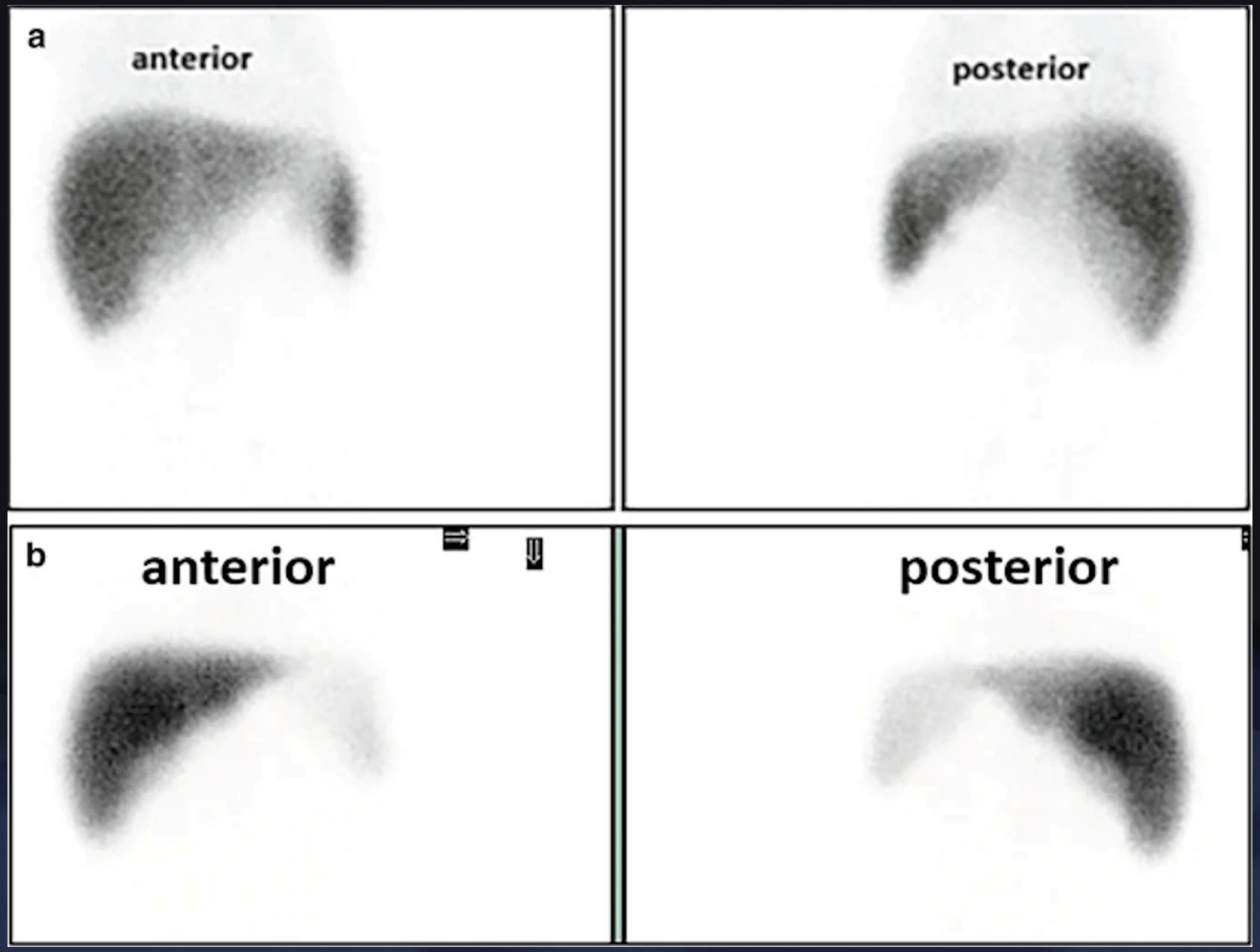
Evaluation of Splenic Function

- **Howell-Jolly bodies** seen when spleen essentially **non-functional**
- **Percentages of pitted/pocked RBCs** can be used to **predict splenic function**
  - Normal spleen - Less than 2%
  - S/p splenectomy - Up to 60%
  - Hyposplenism - Intermediate values

Nuclear Medicine

- Uses relative uptake of technetium-99m sulfur colloid to assess phagocytic function

- **Decreased relative uptake** indicative of **decreased splenic function**


a
anterior
posterior
b
anterior
posterior

Assessment of splenic function

Eur J Clin Microbiol Dis (2010) 29:1456-1473

- "**Function in splenic tissue can temporarily be decreased because of increased disease activity**, while the spleen might actually still be partially functioning and is not in state of atrophy. Assessment of spleen function using **99m-Tc-labelled, heat-altered, autologous erythrocyte scintigraphy** combined with a multimodality SPECT-CT approach seems best for this purpose as **all facets of splenic function are evaluated**."

Assessment of splenic function

Eur J Clin Microbiol Dis (2010) 29:1456-1473

- "Measuring the **clearance rates of 99m-Tc**-labelled, heat-altered, autologous erythrocytes from the circulation should be **considered carefully** as a method of assessing splenic function, since this is **not solely dependent on spleen activity**."

Assessment of splenic function

Eur J Clin Microbiol Dis (2010) 29:1456-1473

- "The population of hyposplenic patients is too large to screen by the use of scintigraphy as a first-line investigation. Therefore, a cheaper, simpler, more accessible method is necessary. At present, we **recommend using the percentage of pitted erythrocytes for this purpose, and refer patients with abnormal percentages for scintigraphy**."

Important Microorganisms

Microorganisms associated with Asplenia

- Encapsulated organisms
- Capnocytophaga canimorsus
- Babes microti

Bacterial Capsule

- Polysaccharide layer surrounding bacterial cell wall
- Protects bacteria from phagocytosis
- Involved in bacterial adherence

Encapsulated Bacteria

Mnemonic: Please SHiNe my SKiS

- P - Pseudomonas aeruginosa (PsA - GNR)
- S - Salmonella species (GNR)
- Hi - Haemophilus influenza type B (HiB - GNR)
- N - Neisseria meningitidis (GN diplococci)
- S - Streptococcus pneumoniae (GPCs in chains/pairs)
- K - Klebsiella pneumoniae (GNR)
- S - Streptococcus agalactiae (GPCs in chains/pairs)

Capnocytophaga canimorsus

GNR

- Associated w/ **dog bites**
  - Most often seen in dog owners & breeders, veterinarians, kennel staff & hunters
- Also associated w/ **alcohol abuse**
- First-line antibiotics: **carbapenems** OR **penicillin/beta-lactamase inhibitor** combinations
  - Imipenem, meropenem, piperacillin-tazobactam, ampicillin-sulbactam

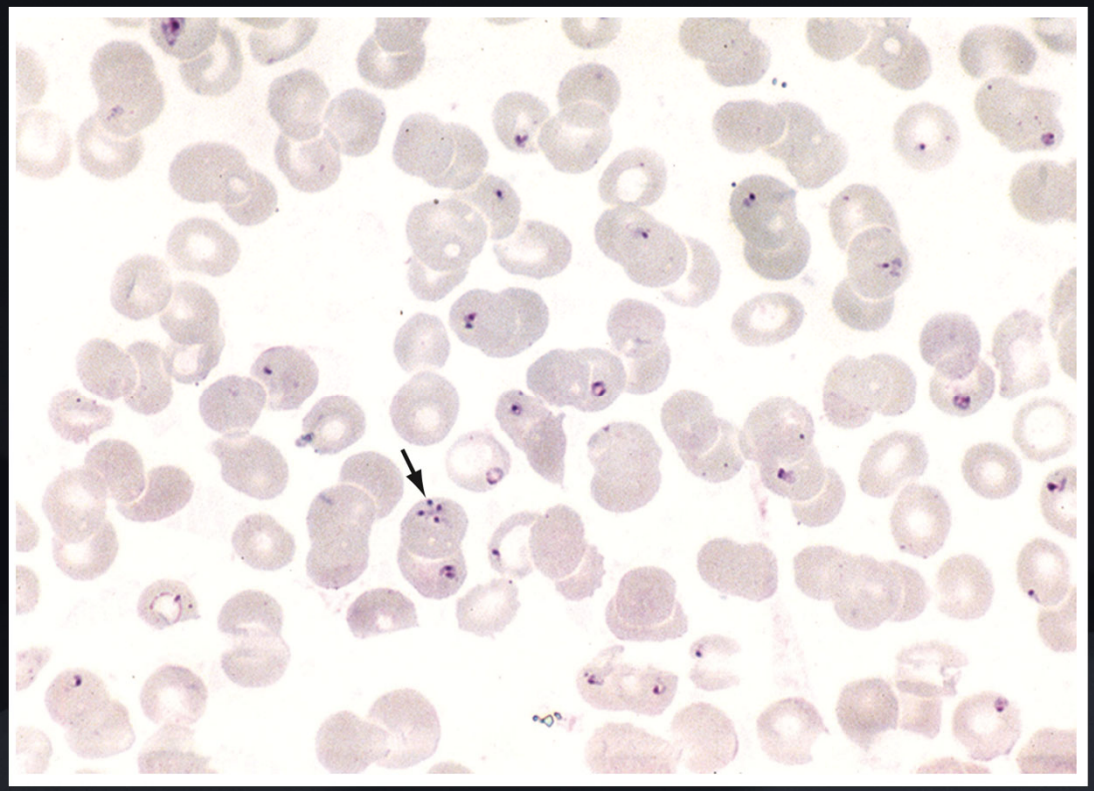
Babesia Species

Hemoprotozoan

- Transmitted via ***Ixodes scapularis*** **tick bite**
- In US, most cases due to **Babesia microti**
- Highest prevalence in **New England & upper Midwest**
- Infection also occurs via **contaminated pRBC** transfusions

Babesia Species

- Presents w/ high fever, chills, sweats, myalgias, anorexia &/or headache
- Associated w/ severe **hemolytic anemia followed by severe thrombocytopenia**
- Definitive diagnosis via **peripheral smear**



Babesia Species

First-line treatment in asplenic patient

- **Atovaquone** 750 mg Q12H PO

- **Azithromycin** 500 mg QD IV

- At least **6 weeks** w/ 2 weeks in which blood smear negative for evidence of infection

Babesia Treatment

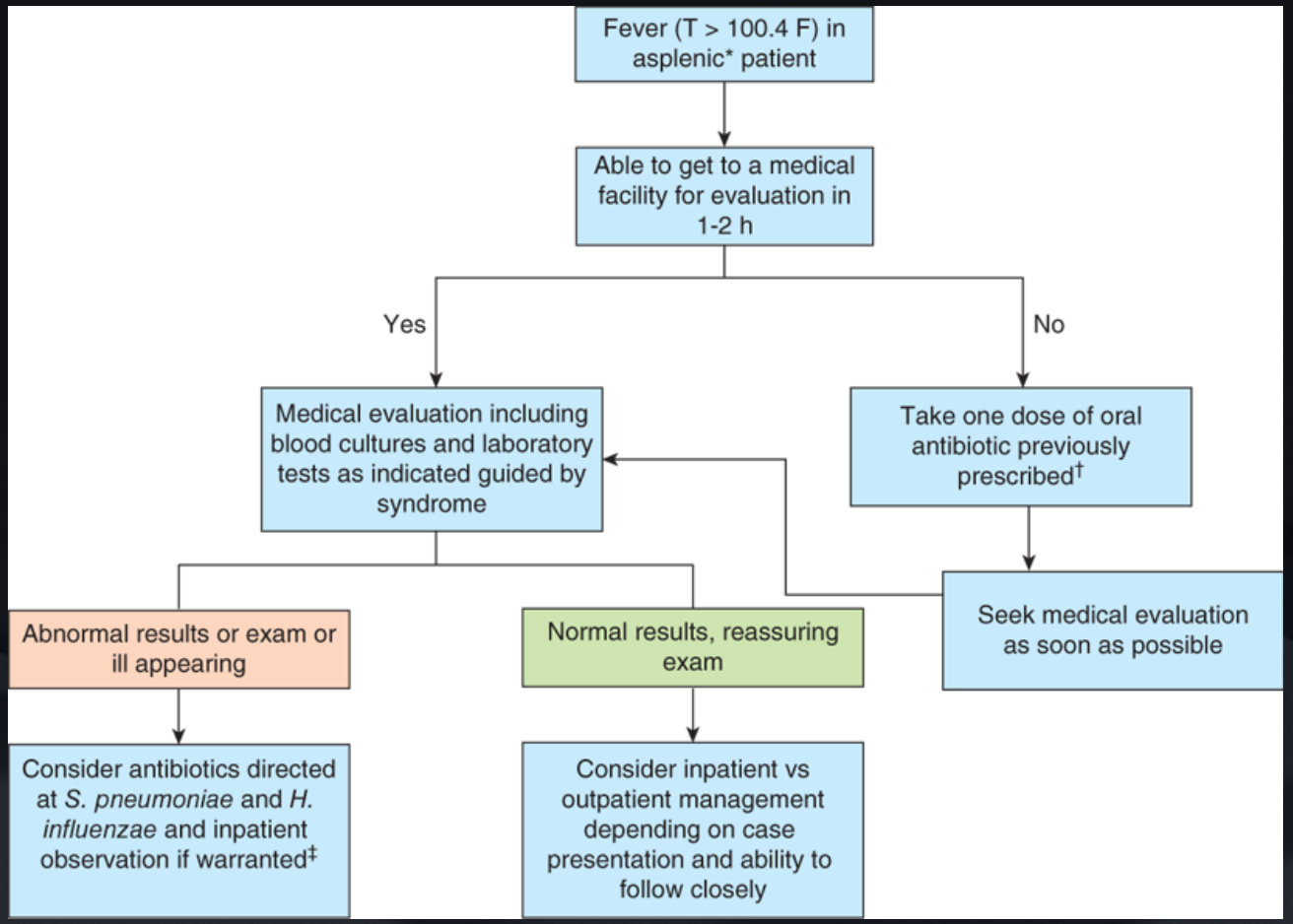
TABLE 281.1 Treatment of Human Babesiosis

SPECIES	ILLNESS	HOST[a]	FIRST-LINE REGIMEN[b]	ALTERNATIVE REGIMEN[b]
Babesia microti	Mild		Atovaquone 750 mg q12h PO plus azithromycin 500 mg PO on day 1 and 250 mg/d PO from day 2 on; for 7–10 d[d]	
	Severe[c]	Immunocompetent	Atovaquone 750 mg q12h PO plus azithromycin 500 mg/d IV[e,f]; for 7–10 d[d]	Clindamycin 600 mg q6h IV plus quinine 650 mg q6–8h PO[f,g,h,i]; for same duration
		Immunocompromised and/or asplenic	Atovaquone 750 mg q12h PO plus azithromycin 500 mg/d IV[j]; for at least 6 consecutive wk, including 2 final wk during which parasites are no longer detected on blood smear[k,l]	Atovaquone 750 mg q12h PO plus clindamycin 600 mg q6h IV with or without azithromycin 500 mg/d IV[m,n]; for same duration

[k]Blood smear is recommended to monitor resolution of infection in severely immunocompromised patients, but recent case reports support the use of a real-time polymerase chain reaction assay to ensure complete parasite clearance.

Fever/Sepsis in Asplenic/ Post-Splenectomy Patients

Fever in Asplenic Patient



Fever / Suspected Sepsis

- **Immediate antibiotics**
- If patient can NOT get medical facility in 1-2 hours, prescribe PO antibiotic dose . . .
  - e.g., amoxicillin-clavulanate (especially if dog bite), cefuroxime, levofloxacin
  - Reasonable to prescribe antibiotics for patients to keep at home in case they develop fever
- . . . then facilitate transportation to medical facility STAT
- IV antibiotics (broad spectrum) & collects **blood cultures STAT**

Empiric Antibiotics

- NOTE: First regimen listed for emergency medical facility (ceftriaxone + vancomycin) would NOT cover Pseudomonas aeruginosa

- So, important to collect history (if able) re: risk factors for Pseudomonas infection

TABLE 311.7 Antibiotic Management Options for Sepsis in Asplenic Patients

CLINICAL SITUATION	DRUGS, ADULT DOSES
Empirical: patient self-administered at onset of fever (before immediate visit to an emergency facility)	Amoxicillin-clavulanate 875 mg PO (q12h) *or* Cefuroxime 500 mg PO (q12h) *or* Levofloxacin 750 mg PO (q24h) *or* Moxifloxacin 400 mg PO (q24h)
Empirical: physician's office (before immediate visit to an emergency facility)	Ceftriaxone 2 g IM or IV *or* Levofloxacin 750 mg PO or IV *or* Moxifloxacin 400 mg PO or IV
Empirical: emergency medical facility	Vancomycin 15-20 mg/kg IV q12h *plus* Ceftriaxone 2 g IV q12h *or* Levofloxacin 750 mg IV q24h *or* Ciprofloxacin 400 mg IV q12h
Definitive: pathogen recovered	Appropriate antibiotic based on culture and antibiotic susceptibility testing

IM, Intramuscular; *IV,* intravenous; *PO,* orally.

TABLE 219.2 Environmental Reservoirs of *Pseudomonas aeruginosa*

Hospital Reservoirs of *P. aeruginosa*

Sinks, taps, showerheads
Potable water
Respiratory therapy equipment
Flower vases, ice makers
Hydrotherapy pools
Cleaning equipment (mops, buckets)
Bronchoscopes, endoscopes
Resuscitators
Water baths
Multidose vials

Community Reservoirs of *P. aeruginosa*

Home humidifiers
Whirlpools, hot tubs, spas
Swimming pools
Water-damaged homes

Asplenic/Post-Splenectomy Sepsis

- Mortality up to 50-70%
- Can present suddenly & progress rapidly to overwhelming septic shock & death
- Most often due to Streptococcus pneumonia infection
  - Present w/ fevers/chills, sore throat, myalgias, vomiting &/or diarrhea
- Can also develop DIC & profound hypoglycemia

Risk Factors

- Age extremes (ie, young & elderly)
- Time since splenectomy/onset of significant splenic dysfunction
  - Increased if temporally closer
- Indication for splenectomy/onset of significant splenic dysfunction
  - Cytopenia > Trauma
- Hemoglobinopathies/Autoimmune disease/Use of immunosuppressants/HIV/Splenic XRT

TABLE 311.3 Risk Factors for Hyposplenia/ Postsplenectomy Sepsis

RISK FACTOR	MECHANISM
Young age	Immune immaturity and naïveté
Old age	Immune senescence, comorbidities
Time since splenectomy	Risk at 0–90 days > 91–365 days > more than 1 year
Indication for splenectomy: splenectomy 2° to immune cytopenias > 2° to trauma > 2° to incidental	Unknown immune dysfunction associated with immune cytopenias
Hemoglobinopathies	Splenic infarction
Lack of appropriate vaccines	Impaired acquired immunity
Immunosuppressive drugs	Immunosuppression
Human immunodeficiency virus–acquired immunodeficiency virus	Immunosuppression
Amyloidosis/sarcoidosis	Splenic infiltration
Autoimmune diseases	Innate immunosuppression
Splenic radiation	Impaired splenic function

Diagnosis & Treatment

- **Blood cultures** are most important test to perform if asplenic sepsis is suspected
  - Can be positive w/in few hours
- **Peripheral blood smear** also important
- If skins purpuric lesions present, collect cultures
- Administer aforementioned **empiric antibiotics & narrow based on culture results**

Notable CDC Vaccine Recommendations

Key Vaccines in Asplenic Patients

(1) Streptococcus pneumoniae (Pneumococcal)

(2) Haemophilus influenza type b (Hib)

(3) Neisseria meningitides (Meningococcal)

(4) Influenza

- If splenectomy is scheduled, CDC recommended vaccines should be administered at least 14 days prior to surgery

Pneumococcal

- If NOT previously vaccinated (PCV13, 15 or 20), vaccine history unknown or only prior PCV7
  - 1 dose of PCV15 or PCV20
- Previously only PCV13
  - 1 dose of PCV20 or PPSV23
- Previously PCV13 & PPSV23
  - 1 dose of PCV20 or PPSV23

Haemophilus influenza type b (Hib)

- 1 dose if previously did not receive Hib vaccine
- If elective splenectomy, 1 dose preferably 14 days prior

Meningococcal

- MenACWY
  - 2-dose series at least 8 weeks apart
  - Revaccinate every 5 years
- MenB
  - 2-dose primary series at least 1 month apart

    . . . OR . . .
  - 3-dose primary series at 0, 1-2 & 6 months
- 1 booster 1 year after primary series & then every 2-3 years

Influenza

- Annually
- Inactivated or recombinant ONLY
- Can NOT receive live-attenuated vaccine

Table 2 Recommended Adult Immunization Schedule by Medical Condition or Other Indication, United States, 2024

Always use this table in conjunction with Table 1 and the Notes that follow. Medical conditions or indications are often not mutually exclusive. If multiple medical conditions or indications are present, refer to guidance in all relevant columns. See Notes for medical conditions or indications not listed.

VACCINE	Pregnancy	Immunocompromised (excluding HIV infection)	HIV infection CD4 percentage and count: <15% or <200mm³	HIV infection CD4 percentage and count: ≥15% and ≥200mm³	Men who have sex with men	Asplenia, complement deficiency	Heart or lung disease	Kidney failure, End-stage renal disease or on dialysis	Chronic liver disease; alcoholism[a]	Diabetes	Healthcare Personnel[b]
COVID-19	See Notes										
IIV4 or RIV4	1 dose annually										
LAIV4					1 dose annually if age 19–49 years				1 dose annually if age 19–49 years		
RSV	Seasonal administration. See Notes	See Notes						See Notes			
Tdap or Td	Tdap: 1 dose each pregnancy	1 dose Tdap, then Td or Tdap booster every 10 years									
MMR	*										
VAR	*			See Notes							
RZV		See Notes									
HPV	*	3 dose series if indicated									
Pneumococcal											
HepA											
Hep B	See Notes									Age ≥ 60 years	
MenACWY											
MenB											
Hib		HSCT: 3 doses[c]				Asplenia: 1 dose					
Mpox	See Notes	See Notes									See Notes

- Recommended for all adults who lack documentation of vaccination, **OR** lack evidence of immunity
- Not recommended for all adults, but recommended for some adults based on either age **OR** increased risk for or severe outcomes from disease
- Recommended based on shared clinical decision-making
- Recommended for all adults, and additional doses may be necessary based on medical condition or other indications. See Notes.
- Precaution: Might be indicated if benefit of protection outweighs risk of adverse reaction
- Contraindicated or not recommended *Vaccinate after pregnancy, if indicated
- No Guidance/ Not Applicable

a. Precaution for LAIV4 does not apply to alcoholism.

b. See notes for influenza; hepatitis B; measles, mumps, and rubella; and varicella vaccinations.

c. Hematopoietic stem cell transplant.

Prophylactic Antibiotics

- Daily PO antibiotics reduce incidence of post-splenectomy sepsis in children
  - American Society of Hematology (ASH) recommends PCN VK BID
- BUT, those are recommendations based studies that were conducted before . . .
  - Increase in penicillin resistance in Streptococcus pneumoniae
  - Before widespread use of conjugated pneumococcal vaccines

Prophylactic Antibiotics

- Similar data re: prophylactic antibiotics in adults lacking

- ASH recommends daily cephalexin or azithromycin prophylaxis for asplenic adults

  . . . BUT . . .

- Does NOT appear that other medical societies/groups agree

Takeaways for Daily Practice

- ***Asplenia / Hyposplenia*** patients are at significantly ***increased risk overwhelming/fatal sepsis, especially w/ encapsulated bacteria, Capnotyophaga & Babesia***
- Hyposplenism associated with/ numerous other diseases such as sickle cell anemia, celiac disease, alcoholic liver disease & IBD
- When presenting w/ fever, asplenic patient need ***HPI-directed antibiotics w/ gram negative coverage w/ blood cultures (& possibly peripheral smear) STAT***
- At discharge, ensure discharge summary recommends outpatient providers address appropriate vaccinations (if patient not up-to-date at admission)

Thank You

Questions?

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