

INFECTION IN THE IMMUNOCOMPROMISED HOST

Sarah P Hammond, MD

Director of Hematology/Oncology Infectious Diseases

Division of Infectious Diseases and Division of

Hematology/Oncology

Massachusetts General Hospital

Assistant Professor of Medicine

Harvard Medical School

Sarah Hammond, MD



- *MD:* Vanderbilt University School of Medicine
- *Residency:* Brigham & Women's Hospital
- *ID Fellowship:* Beth Israel Deaconess Medical Center
- *Transplant ID Fellowship:* Brigham & Women's Hospital/Dana-Farber Cancer Institute
- Director of Hematology-Oncology Infectious Diseases, Massachusetts General Hospital
- Assistant Professor of Medicine, Harvard Medical School
- Research interests: Invasive fungal infection and HBV in immunocompromised patients

Disclosures

- I have research funding from Elion, F2G, Mundipharma and Cidara
- I have consulted for F2G, Pfizer, Treeline Biosciences and Takeda

Overview

- Introduction and Basic Principles
- Drug-induced Immunodeficiency
 - Corticosteroids
 - TNF- α inhibitors
 - JAK inhibitors
 - Anti CD-20 therapy
- Asplenia

Learning Objectives

- To learn about the basic principles of infection in the immunocompromised host
- To learn the best approach to understanding infection risk with immunosuppressive medications
- To learn about infections associated with asplenia and best prevention practices

Introduction and Basic Principles

Infection in Compromised Host

- The immunocompromised host (ICH) is susceptible to opportunistic infections and community-acquired infections
 - Infection can result from exposure to a lower number of organisms
- The inflammatory response to infection is suppressed in ICH
 - Attenuated signs and symptoms of infection
- ICH with infection typically has high burden of organisms once infection established

Basic Principles

- Net state of immunosuppression
 - Dose and duration of suppressive medications
 - Mechanical factors
 - Infections contributing to compromise
- Important epidemiologic exposures
 - New exposures
 - Remote exposures with possibility of reactivation

Fishman JA, Rubin, RH. *N Engl J Med.* 1998;338:1741-51.

Fishman JA. *N Engl J Med.* 2007;357:2601-14.

Drug-Induced Immunosuppression

Mechanism, Indication, Dose & Duration

- The number of immunosuppressants approved to treat malignant and auto-immune disorders is constantly expanding
- Mechanism of an immunosuppressive agent is key to predicting host susceptibility to infection
- Indication for which an agent is given is important when considering impact on host defenses
- Dose and duration over which the agent is given and remains active impacts vulnerability
 - Effect of some biologic agents last for 6 months or more

Immunosuppressive Drugs

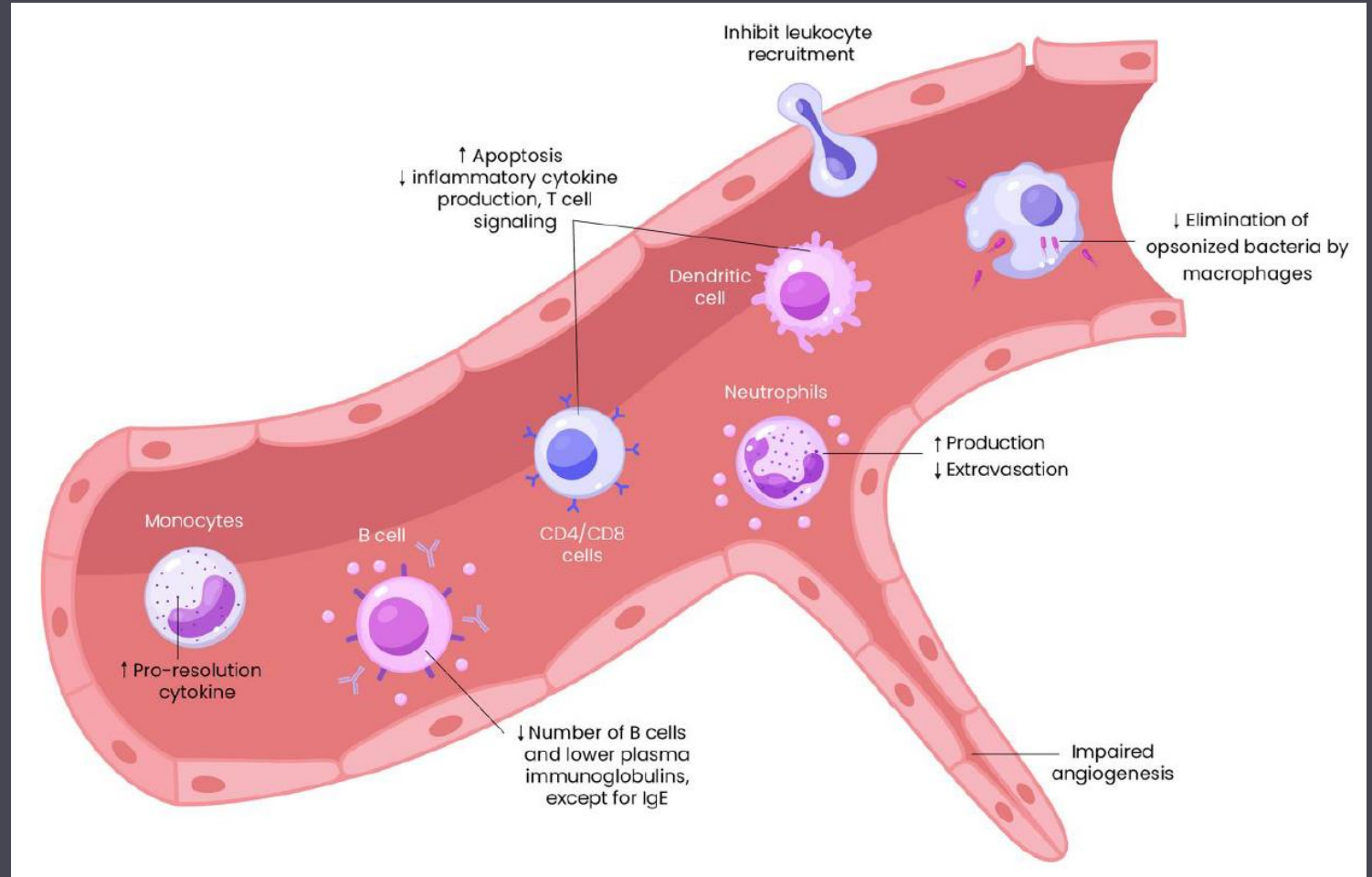
- Corticosteroids
- Antimetabolites
 - Methotrexate
 - Azathioprine, 6-mercaptopurine
 - Mycophenolate
- T lymphocyte agents
 - Tacrolimus, Cyclosporine
 - Sirolimus, Everolimus
- ‘Targeted’ agents
 - Janus kinase inhibitors
 - Ruxolitinib, Baricitinib, Deuruxolitinib
 - Tofacitinib, Upadacitinib, Abrocitinib
- Biological agents
 - IL1 inhibitor
 - Anakinra
 - CTLA-4 analogue
 - Belatacept, Abatacept
- Monoclonal antibodies
 - Tumor necrosis factor- α (TNF- α) inhibitors
 - Infliximab, Adalimumab, Golimumab
 - (Etanercept)
 - Certolizumab pegol
 - CD-20 antibodies
 - Rituximab
 - Ofatumumab, Obinutuzumab
 - Ocrelizumab, Ublituximab
 - C5 complement inhibitors
 - Eculizumab
 - Ravalizumab, Crovalimab
 - Inhibitors of IL-17
 - Secukinumab
 - Ixekizumab
 - Inhibitors of IL-23
 - Guselkumab
 - Risankizumab
 - Ustekinumab

Drug-Induced Immunosuppression

Corticosteroids

Corticosteroids

- Acute effect of corticosteroids on host defenses includes
 - Neutrophil demargination and reduced chemotaxis
 - Lymphopenia and depletion of T lymphocytes
- Long term effect of corticosteroids on host defenses includes
 - Skin weakening and poor wound healing

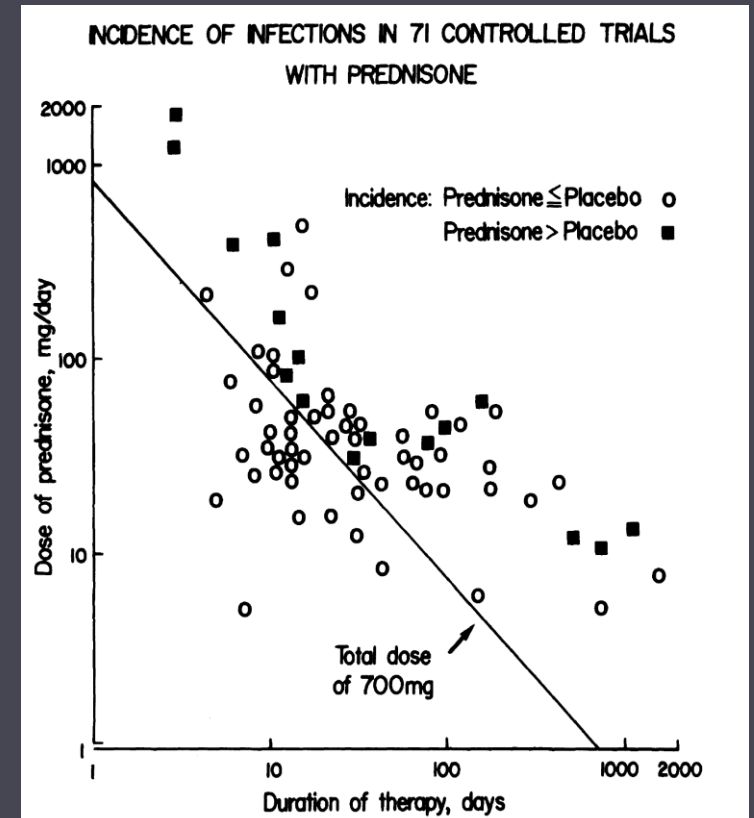


Corticosteroids and infection

- In general, steroids increase risk of infection
 - In controlled studies typically impact is greater on risk of severe/hospitalized infection
- In metanalysis of 71 controlled trials of steroid vs. non-steroid therapy, steroid recipients had significantly higher rate of infection (12.7% vs. 8.0%) and lethal infection (1.2% vs. 0.5%)
 - Included studies of GI, pulmonary, renal, neurologic and rheumatic conditions

Corticosteroids: dose and duration

- In Stuck, et al. metanalysis, steroid dose and duration impacted infection risk
- In large database study of RA, IBD and psoriasis, prednisone doses of <5, 5-10, and >10 mg resulted in a sequential increase in risk of serious infection in RA and psoriasis
- Dose-dependent risk of <10 mg of prednisone per day has been shown in other observational studies



Stuck AE, et al. Rev Infect Dis 1989; 11:954-62.

Grijalva CJ, et al. JAMA 2011;306:2331-9.

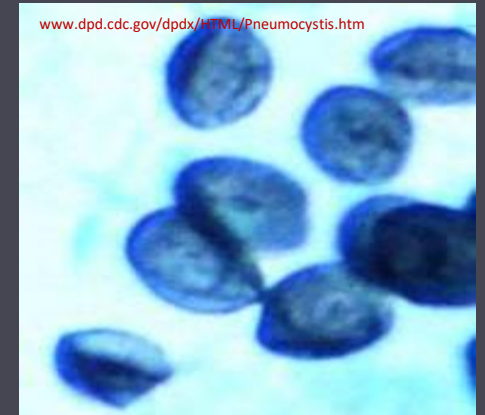
Youssef J, et al. Rheum Dis Clin North Am 2016;42:157-76.

Corticosteroids & Specific infections

- Specific types of infection associated with steroids
 - Opportunistic pathogens
 - Bacterial (eg. Listeria)
 - Fungal (eg. Cryptococcus)
 - Viral (eg. Zoster)
 - Reactivation of latent tuberculosis
 - Strongyloides hyperinfection syndrome
 - Pneumocystis jiroveci pneumonia (PCP)

Corticosteroids and PCP

- Steroids are a major risk factor for PCP
 - In a study of 116 non-HIV patients, 10 (91%) were on steroids
 - Similarly, in a study of 134 non-HIV cancer patients with PCP, 116 (87%) were on steroids
- In recent market database study PCP in non-HIV represented large majority (>70%) of infected population
- PCP in non-HIV patients is rare, but is associated with significant mortality
 - Historically mortality approached 45-50% in non-HIV population, but recent database/coding studies suggest it's lower now
 - One recent study showed mortality in non-HIV population was 7%, but >10% in select patient types (eg. Malignancy)
 - Another study of ~9000 hospitalizations 2019-2022 showed in-hospital mortality was 24% vs. 11% among HIV patients



Corticosteroids and PCP

- PCP risk depends on steroid dose and duration
 - Among 105 non-HIV patients with PCP on steroids
 - Median dose: 30 mg prednisone per day (25% on 16 mg/day or less)
 - Median duration: 12 weeks (25% on for 8 weeks or less)
- PCP risk may not be uniform among patient types
 - In general, risk in lupus, temporal arteritis and rheumatologic disease all linked to 'high dose' steroids (30-50 mg/day)
 - Risk may be especially high in patients with metastatic cancer on steroids
 - PCP risk is elevated, but occurs infrequently in IBD

Yale SH, Limper AH. Mayo Clin Proc 1996;71:5-13.
Sepkowitz KA, et al. JAMA 1992;267:832-7.
Youssef J, et al. Rheum Dis Clin North Am 2016;42:157-76.

Chew LC, et al. J Clin Rheumatol 2015;21: 72–75
Cotter TG, et al. Clin Gastroenterol Hepatol 2017;15:850-6.
Schoovaerts K, et al. Acta Clin Belg. 2017;27:1-4.
Park JW, et al. Ann Rheum Dis 2018;77:644–649.

Corticosteroids and PCP: Prophylaxis

- Stern, et al. performed a metanalysis of PCP prophylaxis studies performed in non-HIV immunocompromised hosts (solid organ transplant, hematologic malignancy)
 - Among 1000 patients from 10 trials of trimethoprim-sulfa prophylaxis compared to no effective therapy, PCP prophylaxis reduced risk by 85% (RR 0.15)
 - The study also showed a significant reduction in mortality attributed to PCP (though did not hold for all cause mortality)
 - Number needed to treat to prevent 1 case PCP was 19 (with study incidence 6%)
- At what steroid dose/duration should prophylaxis start?
 - There are no large trials directly assessing this beyond the metanalysis above
 - Extrapolating from available data many clinicians start prophylaxis after 3-4 weeks of 15-30 mg prednisone per day

Yale SH, Limper AH. Mayo Clin Proc 1996;71:5-13.

Stern A, et al. . *Cochrane Database Syst Rev* 2014, DOI: 10.1002/14651858.CD005590.pub3.

Chastain DB, et al. Clin Infect Dis. 2024;78:e37-e56.

Drug-Induced Immunosuppression

TNF- α Inhibitors

Case Presentation #1

- 55-year-old woman with rheumatoid arthritis (RA) presents with 3 days of productive cough and progressive dyspnea
 - She has had fever as high as 100.9 for last 2 days
- Medical History: RA diagnosed 15 years ago
 - Currently on prednisone 5 mg/daily, infliximab and methotrexate x10 years
- Lives with her husband in rural MA; works remotely in publishing
 - Has a pet dog who she walks outside in a wooded area daily
- Exam
 - T 100.7 F, P 112, R 21, O2 sat 93% 4L nasal canula
 - Notable for tachycardia and coarse crackles in both lungs
- Labs: WBC 15.3 with 79% neutrophils, 7% bands
- Radiology: Chest x-ray shows dense infiltrates in right upper and left lower lobes

Chest CT Scan



Which is the most likely cause of pneumonia?

- A. Legionella pneumophila
- B. Anaplasma
- C. Pneumocystis jirovecii
- D. Influenza
- E. Mycobacterium tuberculosis

TNF- α inhibitors

- TNF- α is an inflammatory cytokine produced by macrophages
 - Important for control of infection with intracellular organisms and for granuloma formation
- There are 5 FDA-approved drugs that inhibit TNF- α
 - Monoclonal antibodies that bind TNF- α : Infliximab (1998), Adalimumab (2002), Golimumab (2009)
 - Pegylated portion of a monoclonal antibody that binds TNF- α : Certolizumab pegol (2008)
 - TNF- α receptor that binds soluble TNF- α : Etanercept (1998)
- ‘Biosimilars’ are biological products that are very similar to approved agents– improved cost/availability
 - FDA has approved **multiple** biosimilars for infliximab, etanercept and adalimumab

TNF- α inhibitors and infection

- Several studies and registries have assessed if TNF- α inhibitors increase overall risk of infection
 - Many studies have assessed risk for bacterial infection; results have been mixed
 - Metanalysis including 9 trials assessed infection risk in RA patients treated with infliximab or adalimumab vs. non-TNF- α therapy
 - Pooled odds ratio for serious infection: 2.0 (95% confidence interval 1.3, 3.1)
 - **Most infections in this study were bacterial (114 of 126)**
 - Limited by control comparison: All controls got placebo (+/- methotrexate, at same dose as TNF- α recipients)

Bongartz T, *et al.* JAMA. 2006;295:2275-85.

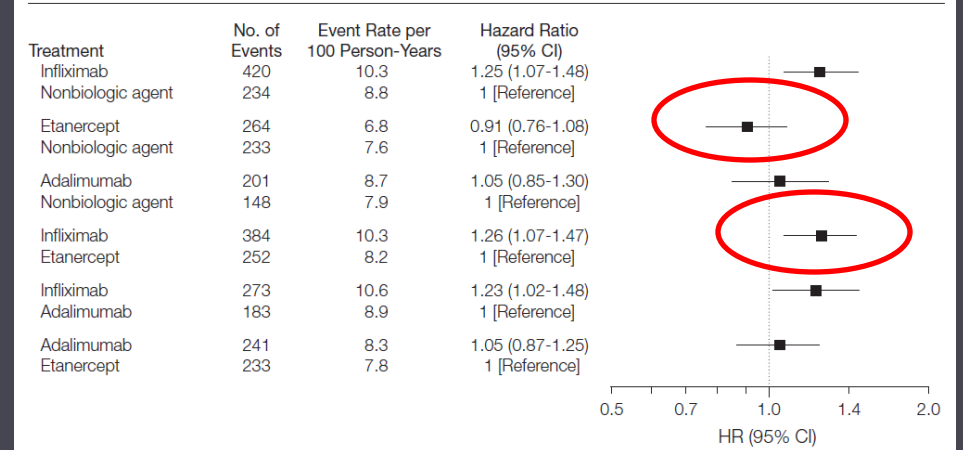
Curtis JR, *et al.* Arthritis Rheum. 2007;56:1125-33.

Schneeweiss S, *et al.* Arthritis Rheum. 2007;56:1754-64.

Infections with TNF- α inhibitors vs. comparators

- Grijalva, et al. assessed infection requiring hospitalization in 16,022 patients with autoimmune disorders treated with infliximab, etanercept or adalimumab vs. non-biologic comparators **1998-2007**
 - Propensity score analysis showed no difference in serious infection in those treated with TNF- α inhibitor vs. comparators for patients with RA, IBD, or psoriasis/spondyloarthritis
 - Among the 10,484 patients with RA, those treated with infliximab had higher risk for serious infection than other TNF inhibitors
- Pawar, et al. studied serious infection in 130,718 RA patients starting tofacitinib vs. other biological agents in **2012-2018**
 - The risks were similar with tofacitinib compared to *most* TNF- α inhibitors, abatacept and tocilizumab

Figure 3. Incidence Rates and Hazard Ratios for Specific TNF- α Antagonists and Serious Infections Among Patients With Rheumatoid Arthritis



Grijalva CJ, et al. JAMA 2011;306:2331-9.
Pawar A et al. Lancet Rheumatol 2020;
2: e84-98

TNF- α inhibitors & Opportunistic Infection

- TNF- α inhibitors have been associated with several opportunistic infections (OIs)
- TB is the most common OI internationally
- In large US database study that included 33,324 new TNF- α users, Pneumocystis was the most common OI

Winthrop KL, et al. Ann Rheum Dis. 2013;72:37-42..
Slifman NR, et al. Arthritis Rheum. 2003;48:319-24.
Perez-Alvarez R, et al. Medicine. 2011;90:359-71.
Salmon-Ceron D, et al. Ann Rheum Dis. 2011;70:616-23.
Baddley JW, et al. Ann Rheum Dis. 2014;73:1942-8.

Table 2 Distribution of non-viral OI (n=80) among new TNFI users for all disease indications*

Infection	Frequency (%)
Pneumocystosis	16 (20)
Nocardiosis/actinomycosis	12 (15)
tuberculosis	10 (12.5)
Histoplasmosis	9 (11.3)
Non-tuberculous mycobacteria	9 (11.3)
Salmonellosis	8 (10)
Listeriosis	4 (5)
Legionellosis	4 (5)
Cryptococcosis	3 (3.8)
Endemic fungal infection *	1 (1.3)
Toxoplasmosis	1 (1.3)
Coccidioidomycosis	1 (1.3)
Blastomycosis	1 (1.3)
Aspergillosis	1 (1.3)

TNF- α inhibitors & Opportunistic Infection

- In French registry study of infliximab, adalimumab and etanercept incidence of OI was low (152 OIs per 100,000 patient-years)
 - Severity of illness was high
 - Median time to OI was 16.2 months (range 6-26)
 - OI risk significantly higher with infliximab compared to etanercept
- In US database study of same TNF- α inhibitors, incidence of non-viral OIs was also low (2.7 OIs per 1000 patient-years), but was significantly higher than patients treated with non-biologic therapy
- In both studies OI risk significantly higher in those on current steroids (>10 mg prednisone/day)

Winthrop KL, et al. *Ann Rheum Dis*. 2013;72:37-42.
Slifman NR, et al. *Arthritis Rheum*. 2003;48:319-24.

Perez-Alvarez R, et al. *Medicine*. 2011;90:359-71.
Salmon-Ceron D, et al. *Ann Rheum Dis*. 2011;70:616-23.
Baddley JW, et al. *Ann Rheum Dis*. 2014;73:1942-8.

TNF- α inhibitors and TB

- Keane, et al. analyzed all cases of TB associated with infliximab reported to FDA 1998-2001
 - 40/70 (57%) had extrapulmonary TB
 - Median time to TB: 12 weeks
- Increased risk demonstrated in more recent large database studies from Europe and US
 - These studies highlight differences in TB risk after monoclonal antibodies vs. etanercept
 - TB risk after infliximab is comparable to adalimumab but both are higher than after etanercept
 - TB develops earlier after infliximab than etanercept (~3 vs 12 months)
- More recent analysis of TB in US patients 2010-2017 who received TNF- α inhibitors showed that extrapulmonary TB remains more common in TNF- α inhibitor recipients
- When TNF- α therapy is planned, patients should be screened with PPD (≥ 5 mm is reactive) or interferon gamma release assay (IGRA)

Keane J, et al. N Engl J Med. 2001;345:1098-104.

Winthrop KL, et al. Arthritis Rheum. 2005;52:2968-74.

Winthrop, KL. Nat Clin Pract Rheumatol. 2006;2:602-610.

Salmon-Ceron D, et al. Ann Rheum Dis. 2011;70:616-23.

Winthrop KL, et al. Ann Rheum Dis. 2013;72:37-42.

Katrak SS, et al. Open Forum Inf Dis. 2022; ofab641

Drug-Induced Immunosuppression

Janus Kinase Inhibitors

JAK Inhibitors

- Janus kinases (JAKs): a group of 4 kinases that bind to cytokine receptors that activate signals that lead to inflammation and immune activation
 - Complicated impact that *varies depending upon dose and which JAK targeted*

JAK Inhibitor	Year	Inhibits	FDA indications
Ruxolitinib	2011	JAK 1+2	Oral: myelofibrosis, P vera, graft-versus-host disease; topical: atopic dermatitis
Tofacitinib	2013	JAK 1+3	RA, JRA, UC, psoriatic arthritis, ankylosing spondylitis
Baricitinib	2018	JAK 1+2	RA, COVID-19, alopecia areata
Upadacitinib	2019	JAK 1	RA, JRA, UC, crohns, psoriatic arthritis, ankylosing spondylitis, atopic dermatitis
Fedratinib	2019	JAK 2	Myelofibrosis
Abrocitinib	2022	JAK 1	Atopic dermatitis
Pacritinib	2022	JAK 2	Cytopenic myelofibrosis
Ritlecitinib	2023	JAK3	Alopecia areata
Momelotinib	2023	JAK 1+2	Myelofibrosis
Deuruxolitinib	2025	JAK 1+2	Severe alopecia areata

JAK inhibitors and Zoster

- Clinical trials of tofacitinib, baricitinib, upadacitinib and ruxolitinib largely show no increased infection risk requiring hospitalization vs TNF- α inhibitors or methotrexate
- These studies do show a clear increased risk for zoster relative to placebo
 - Risk is consistent in different populations (RA, IBD, psoriasis)
- Curtis, et al. studied zoster among >70,000 RA patients on biologic or targeted therapy
 - Risk higher with tofacitinib than with all other therapies
 - Risk is dose-dependent
- Severity of zoster not increased
- Prevention: vaccination may be key

Winthrop KL. Nature Rev Rheumatol. 2017;13:234-43.

Curtis JR, et al. Ann Rheum Dis 2016;75:1843-1847.

Winthrop KL, et al. J Am Acad Dermatol. 2017;77:302-9.

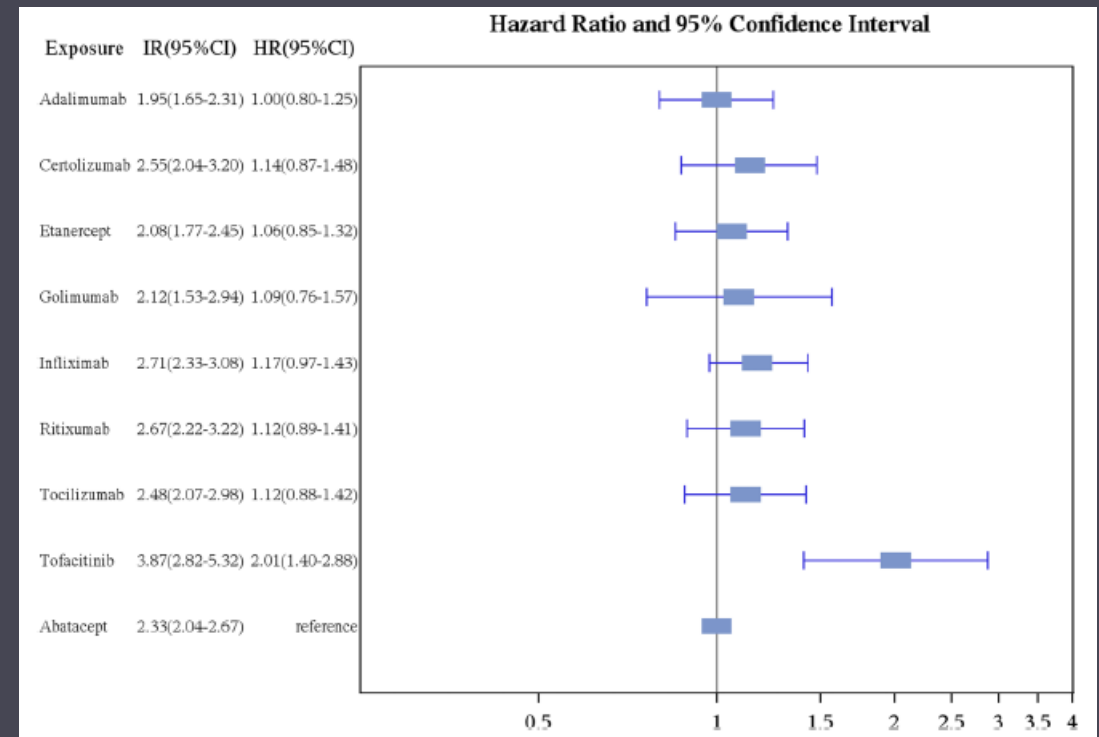
Bechman K, et al. Rheumatology 2019. doi: 10.1093/rheumatology/kez087

Fleishmann R, et al. Arthritis Rheumatol. 2019;71:1788-1800

Pawar A et al. Lancet Rheumatol 2020; 2: e84-98

Winthrop KL, et al. Ann Rheum Dis 2021;80:134-136

Li X, et al. Expert Opin Drug Saf 2025; doi: 10.1080/14740338.2025.2502037.



Drug-Induced Immunosuppression

CD20 Antibodies

Clinical Case #2

- A 58-year-old woman is diagnosed with diffuse large B cell lymphoma (DLBCL) after she presents with several weeks of fevers, night sweats, weight loss and left neck swelling
- Past medical history
 - Hypercholesterolemia
 - An episode of 'hepatitis' requiring a brief hospital stay after she was stuck by a needle when she was training to be a phlebotomist 35 years ago
- Plans are made to initiate chemotherapy with rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP)

Clinical Case #2

- Physical exam is notable for a thin woman with marked left neck lymphadenopathy
- Labs are notable for normal BUN, Cr, AST, ALT, and bilirubin
 - Hepatitis B surface antibody (HBsAb)– 27 IU/L
 - Hepatitis B core IgG (HBcAb) – positive
 - Hepatitis B surface antigen (HBsAg) – negative
 - Hepatitis B virus PCR – negative
 - Hepatitis C virus antibody – positive
 - Hepatitis C virus PCR – negative
 - HIV screening - negative

What is the best management for her previous hepatitis exposures?

- A. Monitor hepatitis C PCR and HBsAb every 2-4 weeks while she is on chemotherapy
- B. Start prophylactic low dose ribavirin and lamivudine to continue for 1 year
- C. Start prophylactic entecavir to continue until 12 months after chemotherapy
- D. No special care is indicated since both hepatitis B and C are old infections that have resolved

CD20 Antibodies

- Rituximab is a monoclonal antibody directed at CD-20, a B lymphocyte marker
 - Immunologic effect is depletion of B lymphocytes
 - Functionally this leads to inability to mount antibody response to new antigens
 - Many studies have shows reduced response to vaccines including Flu and Covid
- FDA approved for treatment of some lymphomas, chronic lymphoid leukemia (CLL), RA, pemphigus vulgaris and a few vasculitides
 - Used off-label to treat other immune-mediated conditions
- Other CD20 antibodies: Ofatumumab, Obinutuzumab, Ocrelizumab, Ublituximab and a few biosimilars to rituximab appear to have same infectious complications
- Novel class of bispecific CD20 antibodies that concurrently target CD3 (T cell activator) recently approved: mosunetuzumab, epcoritamab, glofitamab
 - Unclear if the infectious complications will be the same or augmented

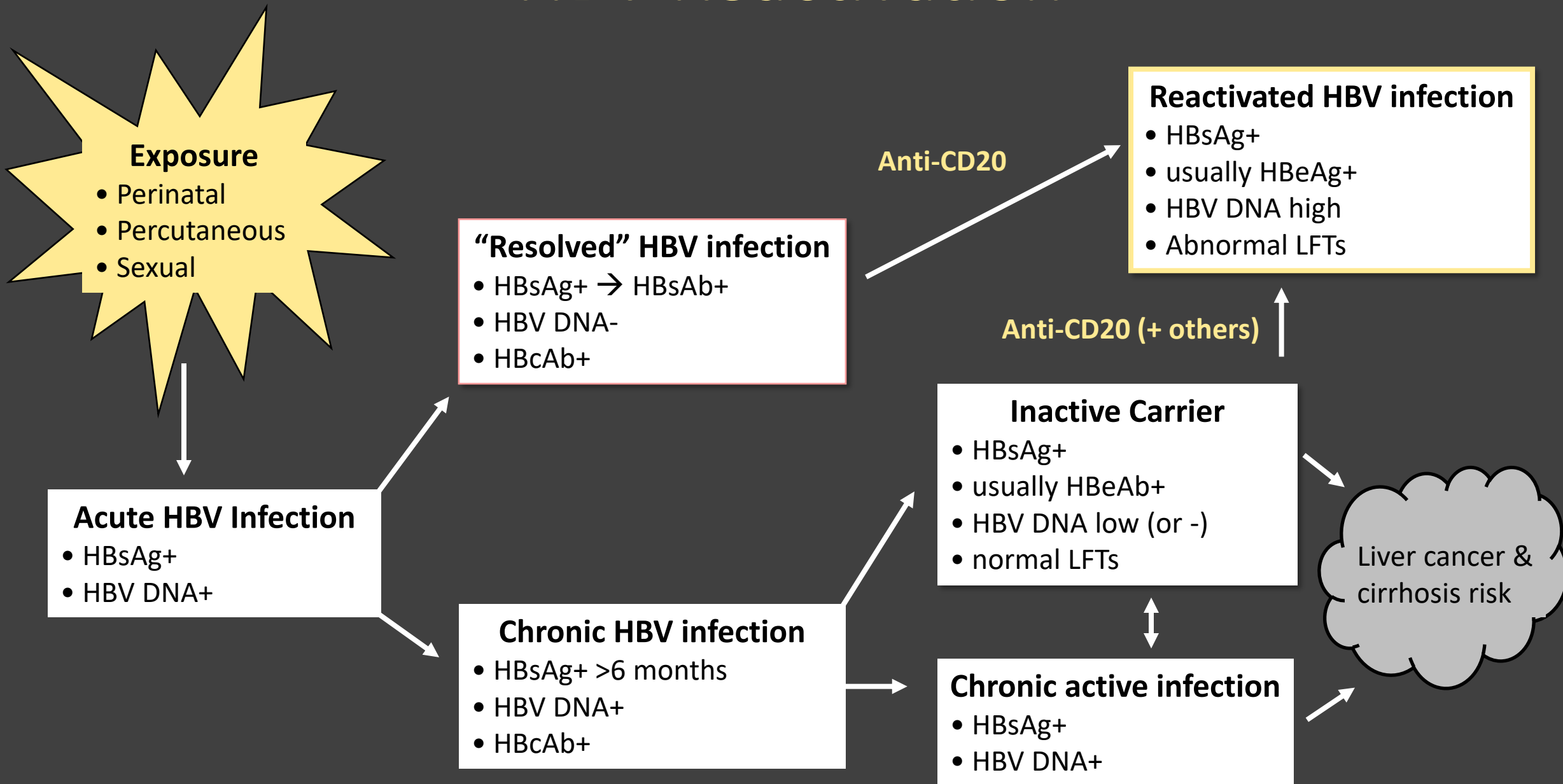
Anti-CD20 and Infection

- Pre-marketing trials of rituximab and ocrelizumab showed no increase in infection in RA/cancer patients and MS patients respectively relative to placebo
- With clinical use, there have been several case reports of various opportunistic infections
 - PCP and Progressive multifocal leukoencephalopathy due to JC virus are most commonly cited in case reports/series
 - Others include CMV reactivation, pure red cell aplasia due to parvovirus, and enterovirus encephalitis
 - Interpretation of case reports is difficult since patients often on multiple immunosuppressants
- Rituximab is definitively associated with
 - Hepatitis B virus (HBV) reactivation
 - Increased severity of babesiosis (in exposed patients)
 - Increased severity/persistence of COVID (in naïve patients?)

Coiffier B, *et al.* N Engl J Med. 2002;346:235-42.
Edwards JCW, *et al.* N Engl J Med. 2004;350:2572-81.
Montalban X, *et al.* N Engl J Med 2017;376:209-20.
Hauser SL, *et al.* N Engl J Med 2017;376:221-34.

Suzan F, *et al.* N Engl J Med. 2001;345:1000.
Sharma VR, *et al.* Blood. 2000;96:1184-6.
Padate BP, Keidan J. Clin Lab Haem. 2006;28:69-71.
Perez-Alvarez R, *et al.* Medicine. 2011;90:359-71.
Kakoullis L, *et al.* Clin Infect Dis. 2025; doi: 10.1093/cid/ciaf034

HBV Reactivation



Rituximab and HBV Reactivation

- Fulminant hepatic failure and death can occur with reactivation with rituximab
 - Reactivation also reported with ofatumumab and ocrelizumab
- Risk of reactivation is higher in chronic carriers (HBsAg+) than in patients with resolved HBV
- Prevention: all patients in whom anti-CD20 therapy, TNF- α inhibitor, or high-dose steroid therapy is being considered should be screened
 - Antiviral prophylaxis typically given to inactive carriers
 - Agents with high barrier to resistance recommended
 - Management of HBcAb+ patients varies
 - Guidelines advocate for prophylaxis, though recent studies have shown that careful monitoring with preemptive therapy is also reasonable if meticulous lab follow up is feasible

Terrault NA, et al. Hepatology. 2018;67:1560-99.
Perez-Alvarez R, et al. Medicine. 2011;90:359-71.
Kusumoto S, et al. Clin Infect Dis 2015;61:719-29.
Hwang JP, et al. J Clin Oncol 2020;38: 3698-3715

FS Ali, et al. Gastroenterol. 2025;168:267–84.
Kusumoto S, et al. Blood. 2019;133:137-146.
Hicks LK, Feld JJ. Blood. 2019;133:104-6.
Ciardi MR, et al. Open Forum Inf Dis. 2019;6:ofy356.

CD20 Antibodies and Babesiosis



- A tick-borne malaria-like parasitic infection endemic to Northeastern US, Wisconsin and Minnesota
 - Causes fevers, malaise, hemolytic anemia and thrombocytopenia
- Patients treated with CD20 antibodies (and other B cell suppressing agents and/or splenectomy) who acquire babesia shortly before or after treatment have worse illness
- CD20 antibody-treated patients with babesiosis:
 - Often have a higher parasite burden (median 8% vs. 2.5%)
 - More likely to develop severe complications including AKI and ARDS
 - More likely to have relapse requiring repeat or prolonged treatment (≥ 6 wks)
 - In a recent multicenter retrospective study patients treated with B cell depleting therapies (mostly rituximab) had significantly higher odds of relapse (OR 9.4, CI, 1.6–56.8) relative to other compromised and non-immunocompromised patients

Asplenia

Asplenia

- Immunologically the spleen plays an important role in filtering blood
- Asplenic patients are at risk for overwhelming bacterial infection due to encapsulated organisms: *S. pneumoniae*, *H. influenzae*, *N. meningitidis*
- In recent study of severe sepsis in asplenia, *S. pneumoniae* caused 42% of infections (most invasive), more than any other pathogen
 - No cases of *H. influenzae* or *N. meningitidis* observed
- Progression of infection can be rapid with high mortality
 - Risk varies by reason for and time since splenectomy as well as knowledge of risk
- Other infections linked to asplenia: *Capnocytophaga canimorsus* (oral flora of dogs) and increased severity of babesiosis

LG Rubin, W Schaffner. NEJM 2014;371:349-56
MS El-Alfy, MH El-Sayed. Hematol Journal 2004;5:77-80
Theilacker C, et al. Clin Infect Dis. 2016;62:871-8

Stiegler D, et al. Am J Forensic Med Pathol. 2010;31:198-9.
Davidson RN, Wall RA. Clin Microbiol Infect. 2001;7:657-60.
Krause PJ, et al. Clin Infect Dis. 2008;46:370-6.
Kakoullis L, et al. Clin Infect Dis. 2026; doi: 10.1093/cid/ciaf034

Vaccination of Asplenic Patients

- Vaccination for *S. pneumoniae*, *H. influenzae*, and *N. meningitidis* crucial to prevent infection
- Timing with splenectomy
 - Vaccinate at least 2 weeks pre-splenectomy in planned cases and 1-2 weeks after (or before hospital discharge) in unplanned cases
- Vaccination algorithms
 - *S. pneumoniae*: One dose 20-valent or 21-valent conjugate pneumococcal vaccine; if one dose of 15-valent conjugate vaccine given follow with 23-valent polysaccharide vaccine given a minimum of 8 weeks later
 - *N. meningitidis*: two vaccine series now also recommended include conjugate meningococcal ACWY and meningococcus type B
 - *Hemophilus influenza*: one dose, preferably 14 days before elective splenectomy

For guidance for patients who previous got other pneumococcal vaccines:
<https://www.cdc.gov/vaccines/hcp/imz-schedules/adult-notes.html#note-pneumo>; accessed 7/9/2026

Davidson RN, Wall RA. Clin Microbiol Infect 2001;7:657-60.
LG Rubin, W Schaffner. NEJM 2014;371:349-56
<https://www.cdc.gov/vaccines/hcp/imz-schedules/adult-medical-condition.html>; accessed 7/9/2026

Management of fever

- Education about risk of severe bacterial infection is key driver of asplenic patients having lower infection risk
 - Survey studies show 5-25 % of asplenic patients have poor knowledge of infection risk
 - In one study overwhelming infection occurred in 16.9% of 79 asplenic patients with poor knowledge vs. <2% of 142 with good knowledge
- “Pill in pocket” approach

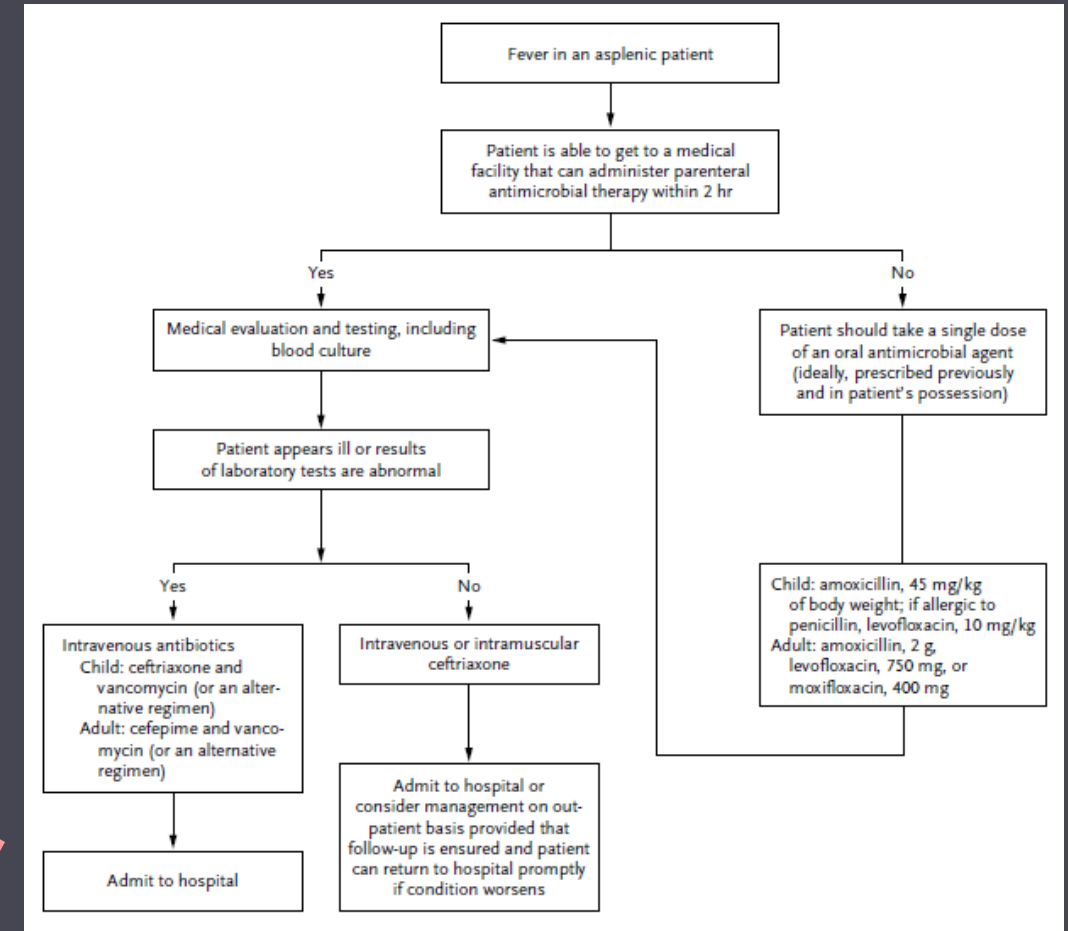


Figure 1. Management of an Episode of Fever in an Asplenic Patient.

Abnormal results of laboratory tests would include a markedly high or low leukocyte count, a leftward shift (immaturity) in the leukocyte differential count, or a low platelet count.

Summary Take-Away Points

(for MOC reflective statement)

- ICH with infection often presents with attenuated signs and symptoms of infection
- When treating an ICH with infection consider:
 - Net state of immunosuppression
 - Includes mechanism, indication, dose/duration for patients on suppressive medications
 - Epidemiologic exposures
- Asplenia increases risk for overwhelming bacterial infection→
vaccinate and educate about fever

Selected References

- Fishman JA, Rubin RH. N Engl J Med. 1998;338:1741-51.
- Chastain DB, et al. Clin Infect Dis. 2024;78:e37-e56.
- Davis JS, et al. Clin Microbiol Rev 2020;33:e00035-19.
- Rubin LG , Schaffner W. N Engl J Med. 2014;371:349-56.

Disclosures

- I have research funding from Elion, F2G, Mundipharma and Cidara
- I have consulted for F2G, Pfizer, Treeline Biosciences and Takeda