

# INFECTION IN THE IMMUNOCOMPROMISED HOST

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# Overview

- Introduction and Basic Principles
- Drug-induced Immunodeficiency
  - Corticosteroids
  - TNF- $\alpha$  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



# 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

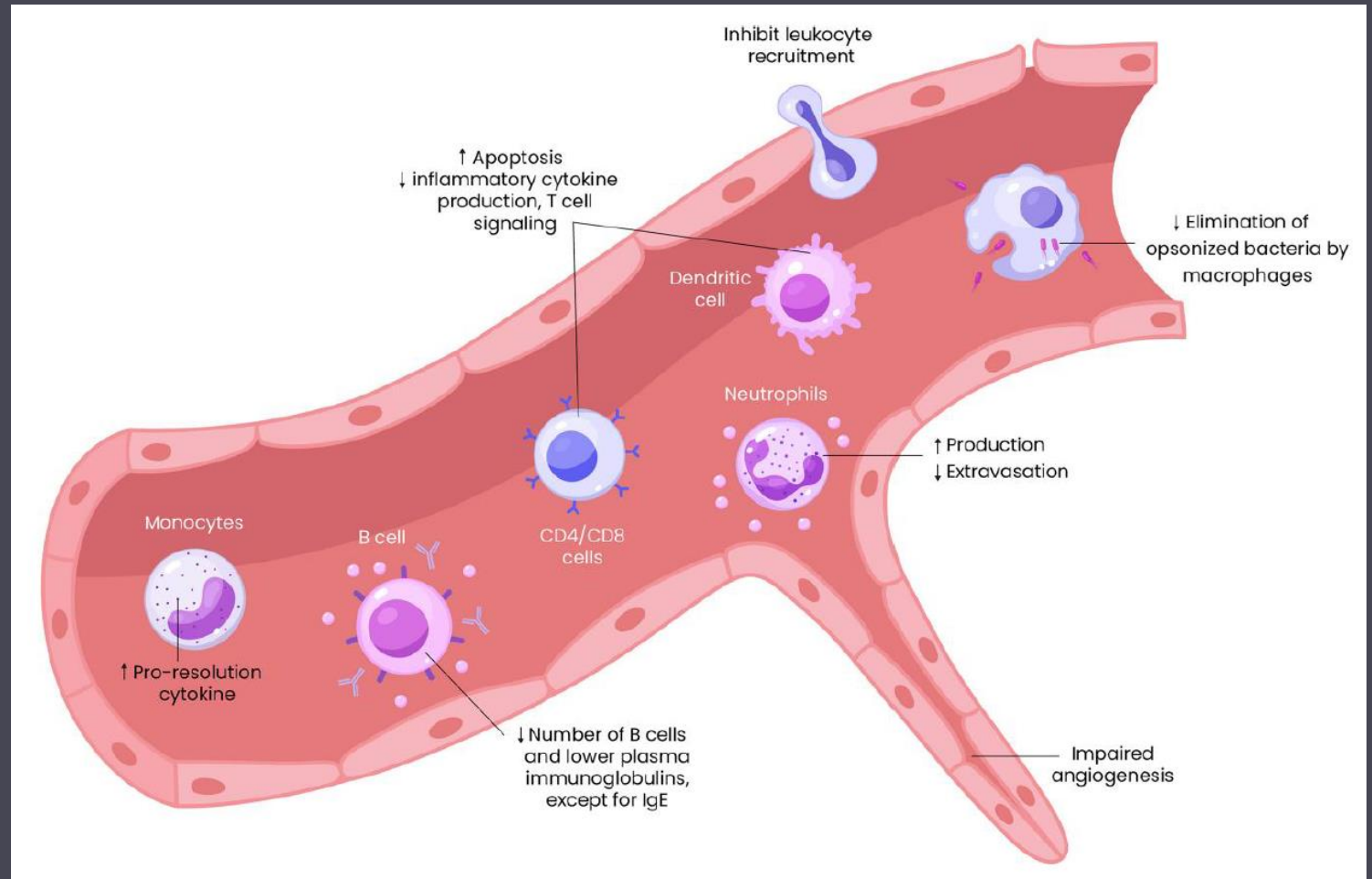
- Corticosteroids
- Antimetabolites
  - Methotrexate
  - Azathioprine, 6-mercaptopurine
  - Mycophenolate
- T lymphocyte agents
  - Tacrolimus, Cyclosporine
  - Sirolimus, Everolimus
- ‘Targeted’ agents
  - Janus kinase inhibitors
    - Ruxolitinib, Baricitinib, Deuruxolitinib
    - Tofacitinib, Upadacitinib, Abrocitinib
- Biological agents
  - IL1 inhibitor
    - Anakinra
  - CTLA-4 analogue
    - Belatacept, Abatacept
- Monoclonal antibodies
  - Tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) inhibitors
    - Infliximab, Adalimumab, Golimumab
    - (Etanercept)
    - Certolizumab pegol
  - CD-20 antibodies
    - Rituximab
    - Ofatumumab, Obinutuzumab
    - Ocrelizumab, Ublituximab
  - IL6 receptor antibody
    - Tocilizumab, sariliumab
  - C5 complement inhibitors
    - Eculizumab
    - Ravalizumab, Crovalimab
    - (Nomacopan, Zilucoplan)
    - (Avacopan)
- Bispecific antibodies
  - CD19/CD3 antibodies
  - B cell maturation antigen/CD3 antibodies

# 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

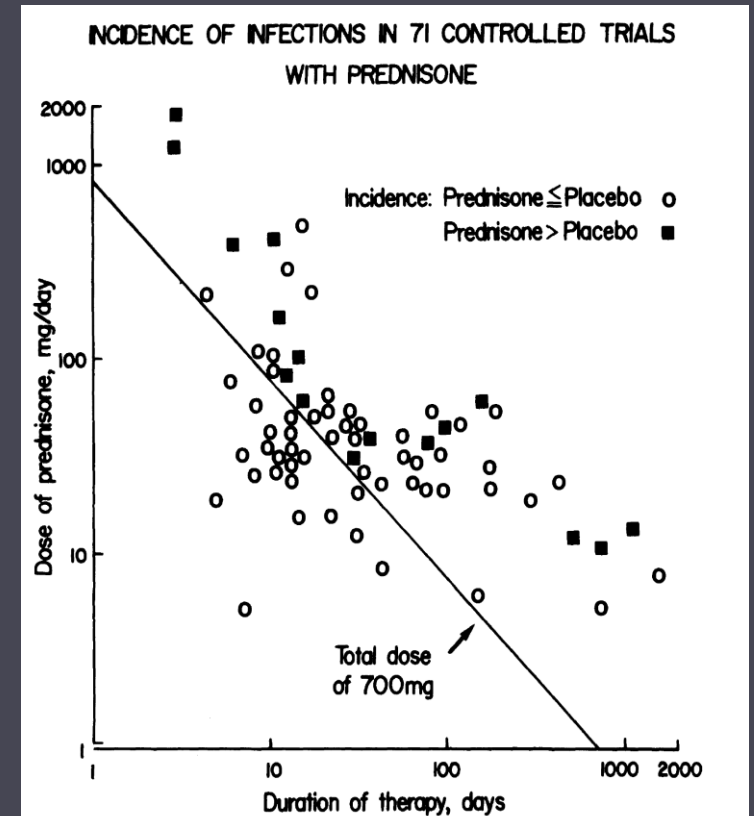


# Corticosteroids and infection

- 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.

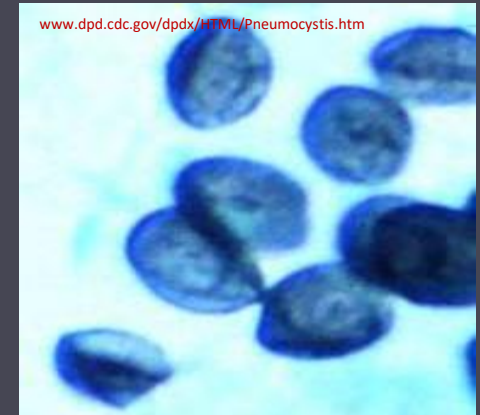
# Corticosteroids & Specific infections

- 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

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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- $\alpha$  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- $\alpha$ inhibitors

- TNF- $\alpha$  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- $\alpha$ 
  - Monoclonal antibodies that bind TNF- $\alpha$ : Infliximab (1998), Adalimumab (2002), Golimumab (2009)
  - Pegylated portion of a monoclonal antibody that binds TNF- $\alpha$ : Certolizumab pegol (2008)
  - TNF- $\alpha$  receptor that binds soluble TNF- $\alpha$ : 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



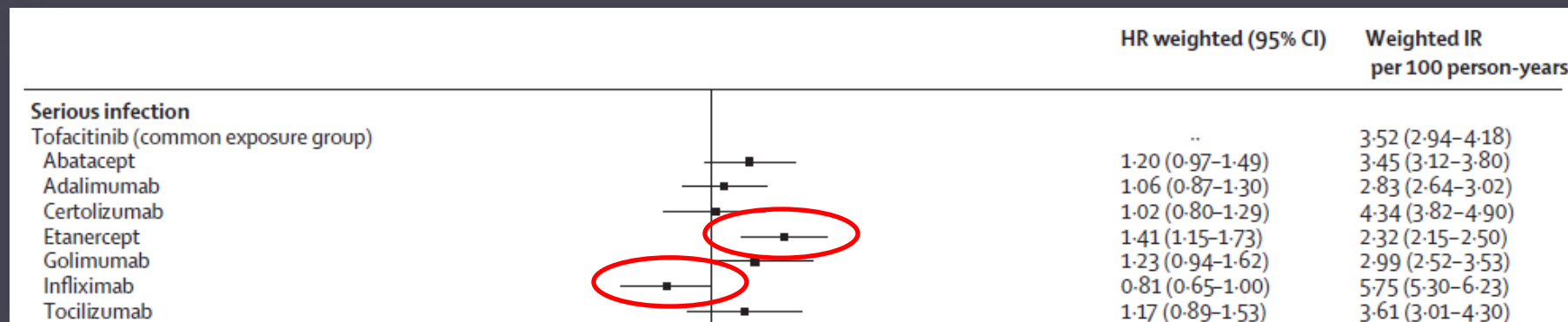
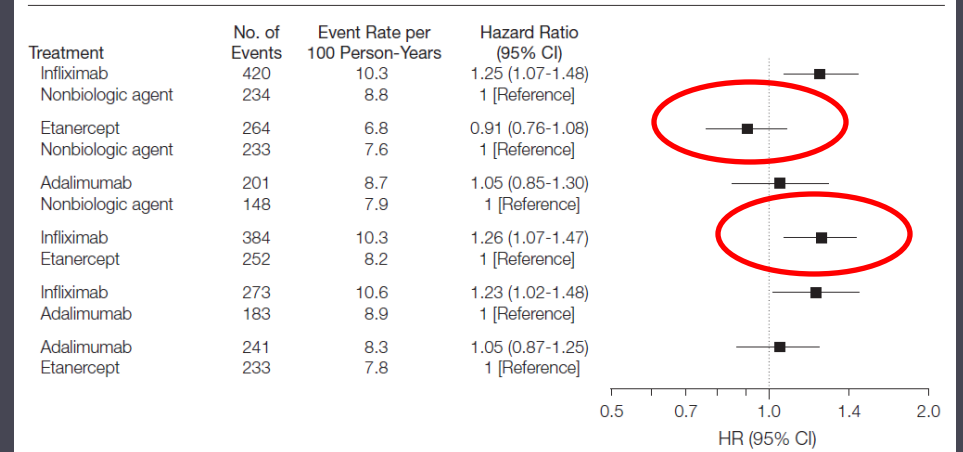
# TNF- $\alpha$ inhibitors and infection

- Several studies and registries have assessed if TNF- $\alpha$  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- $\alpha$  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-  $\alpha$  recipients)

# Infections with TNF- $\alpha$ 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- $\alpha$  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- $\alpha$  inhibitors, abatacept and tocilizumab

**Figure 3.** Incidence Rates and Hazard Ratios for Specific TNF- $\alpha$  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- $\alpha$ inhibitors & Opportunistic Infection

- TNF- $\alpha$  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- $\alpha$  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- $\alpha$ 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- $\alpha$  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- $\alpha$ 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- $\alpha$  inhibitors showed that extrapulmonary TB remains more common in TNF- $\alpha$  inhibitor recipients
- When TNF- $\alpha$  therapy is planned, patients should be screened with PPD ( $\geq 5$ 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	<b>Oral:</b> myelofibrosis, P vera, graft-versus-host disease; <b>topical:</b> 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- $\alpha$  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.

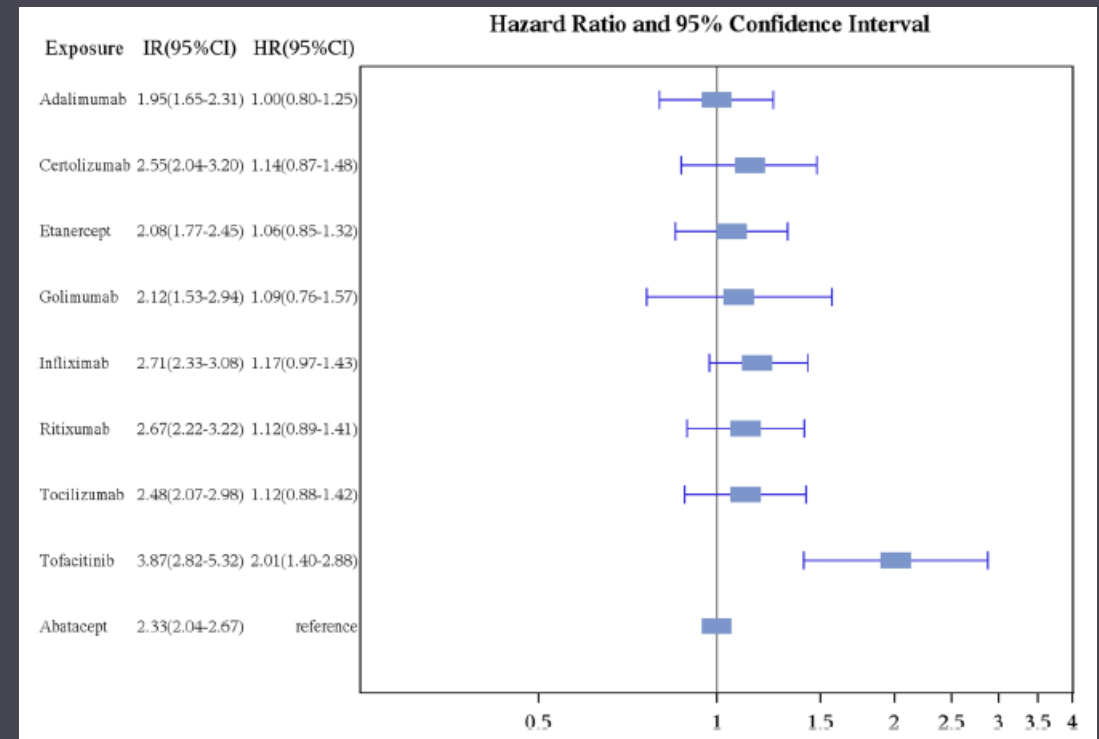
Bechman K, et al. Rheumatology 2019. doi: 10.1093/rheumatology/kez087

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 and recall 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 including 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

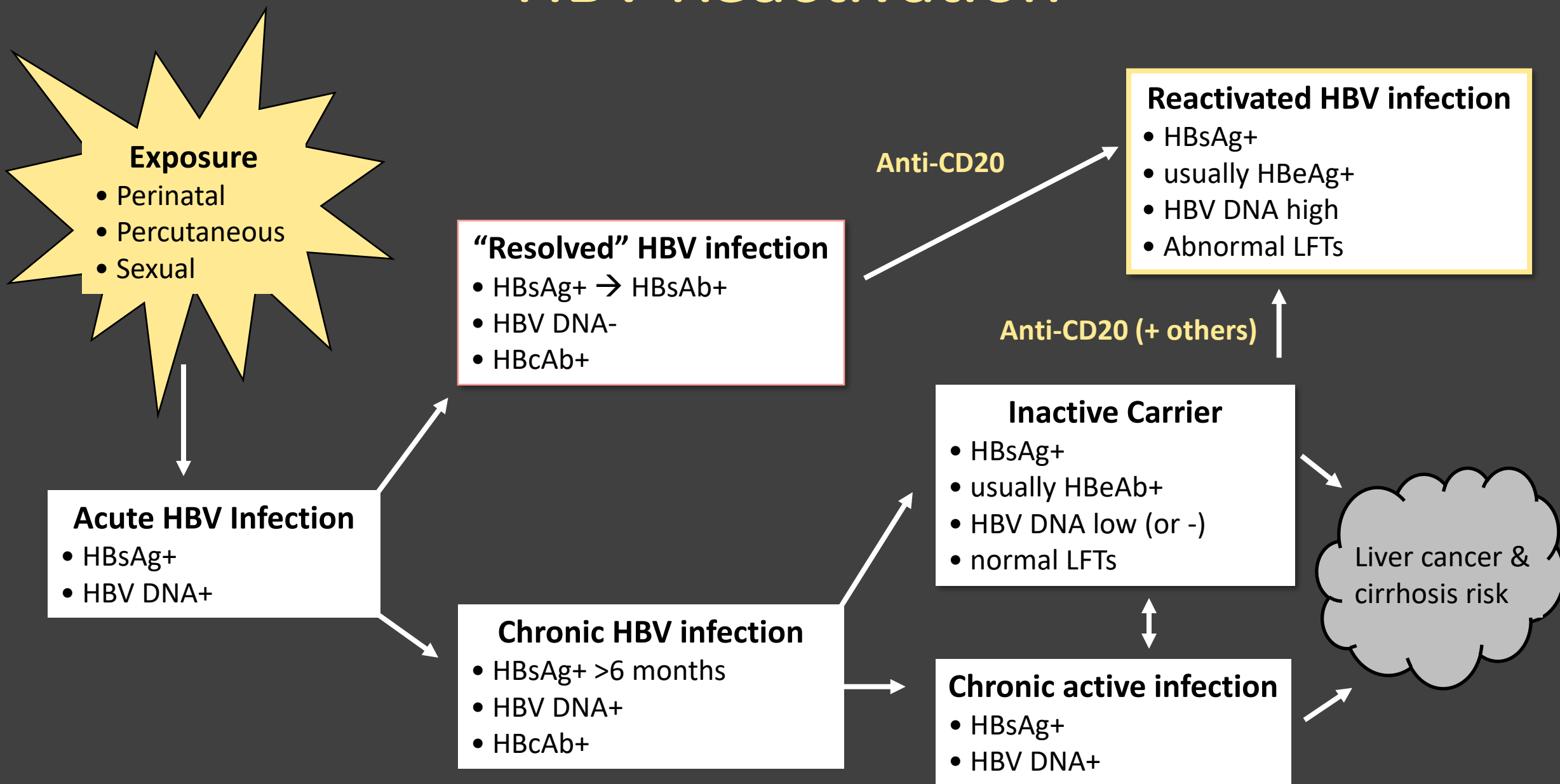
# Anti-CD20 and Infection

- 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/persistence of COVID
  - Increased severity of babesiosis (in exposed 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.  
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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- $\alpha$  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

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# CD20 Antibodies and Covid

- Multiple studies have shown CD20 therapy is associated with increased risk of severe covid or death from covid relative to comparators in patients with rheumatologic disease and multiple sclerosis
  - A global registry study showed marked increase in risk for RA patient on rituximab vs. TNF inhibitors

COVID-19 outcome	Abatacept		Rituximab		IL-6 Inhibitors		JAK inhibitors		TNF inhibitors
	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value	
Hospitalised	1.18 (0.76 to 1.82)	0.47	4.53 (3.32 to 6.18)	<0.01	0.84 (0.53 to 1.33)	0.45	2.40 (1.78 to 3.24)	<0.01	Ref
Hospitalised with oxygenation/ventilation or death	1.12 (0.70 to 1.81)	0.63	2.87 (2.03 to 4.06)	<0.01	0.72 (0.43 to 1.20)	0.20	1.55 (1.04 to 2.18)	0.01	Ref
Death	1.46 (0.72 to 2.89)	0.30	4.57 (3.32 to 9.01)	<0.01	1.13 (0.50 to 2.59)	0.77	2.04 (1.58 to 2.65)	<0.01	Ref
Mechanical ventilation (restricted to only hospitalised patients, n=613)	1.41 (0.94 to 2.10)	0.09	4.05 (3.08 to 5.33)	<0.01	0.75 (0.51 to 1.10)	0.14	2.03 (1.56 to 2.62)	<0.01	Ref
Mechanical ventilation or death	1.14 (0.78 to 1.66)	0.50	4.44 (3.39 to 5.82)	<0.01	0.74 (0.50 to 1.09)	0.12	2.02 (1.56 to 2.61)	<0.01	Ref

\*Adjusted for age, sex, region, calendar time, obesity, smoking, concomitant csDMARD use, glucocorticoid use/dose, comorbidity count, hypertension/cardiovascular disease, interstitial lung disease, cancer and rheumatoid arthritis disease activity.  
 csDMARD, conventional synthetic disease-modifying antirheumatic drug; IL-6, interleukin 6; JAK, Janus kinase; Ref, reference; TNF, tumour necrosis factor.

# CD20 Antibodies and Covid

- Multiple studies have shown CD20 therapy is associated with increased risk of severe covid or death from covid relative to comparators in patients with rheumatologic disease and multiple sclerosis
  - A global registry study showed marked increase in risk for RA patient on ritixumab vs. TNF inhibitors
- Legions of case reports/series describe protracted and morbid cases of Covid in lymphoma patients treated with B cell depleting therapy
  - Patients do not make antibodies to SARS-CoV-2

# 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  
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Kakoullis L, et al. Clin Infect Dis. 2025; doi: 10.1093/cid/ciaf034

# Vaccination of Asplenic Patients

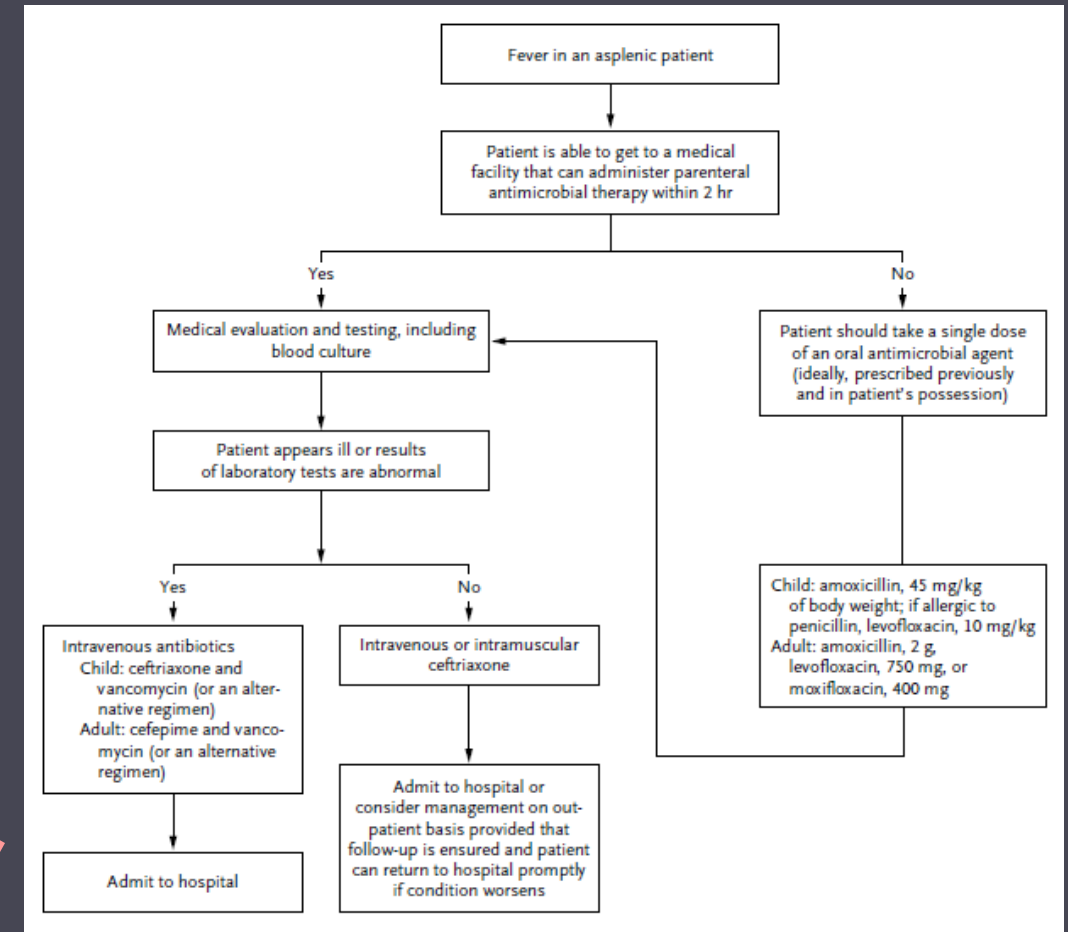
- Vaccination for *S. pneumoniae*, *H. influenzae*, and *N. meningitidis* crucial to prevent infection
- Timing with splenectomy
  - Vaccinate at least 2 weeks pre-splenectomy in planned cases and 1-2 weeks after (or before hospital discharge) in unplanned cases
- Vaccination algorithms
  - *S. pneumoniae*: One dose 20-valent or 21-valent conjugate pneumococcal vaccine or one dose of 15-valent conjugate vaccine followed by 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 7/9/2025

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#table-conditions>; accessed 7/9/2025

# 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

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- I have consulted for Melinta, Pfizer, Roche, Seres Therapeutics, Treeline Biosciences and Takeda