

Vaccinating the Immunocompromised Patient: What to use and what to avoid

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- G. Stiver potential conflicts:

None for this talk.

Objectives

- To know which vaccines to use and which to avoid in immunosuppressed patients with :
- HIV disease
- Chronic renal and hepatic disease
- Rheumatologic diseases
- Inflammatory bowel disease
- Splenectomy
- Solid organ transplants
- Bone marrow (human stem cell) transplants
- Immunosuppressed travellers

What constitutes immunosuppression for the purposes of immunization?

1. Drug Therapy:

- Anyone taking corticosteroids for >2 weeks at doses of >20 mg prednisone per day.
- Patients on:
 - DMARDS – Imuran (azathioprine),
Methotrexate
 - “Biologic DMARDS” – monoclonal Ab

IVIg - delay MMR vaccine 10-11mo

- (e.g for streptococcal toxic shock syndrome, or Stevens-Johnson syndrome) – may inhibit antibody responses to measles and rubella vaccines (no data on mumps) for 10-11 months.

IM Ig- delay MMR vaccine 3-7 months

- HEP A,B, tetanus, measles, VZIG, rabies
Blood incl packed cells, platelet transfⁿ

2. Procedure:

- Chemotherapy and first 3 months after
- Allogeneic human stem cell transplant up to 2 years post transplant.
- Autologous HSCT for 1 year post transplant

- **Antirejection drugs:**
- Anticalcineurin agents
 - Cyclosporin A and Tacrolimus
- Anti-inflammatory or anti-proliferative drugs
 - steroids, Imuran, mycophenylate
- Targeted monoclonal antibodies
 - non-cell-depleting:
daclizumab, basilixumab(anti-IL-2 receptor)
 - cell-depleting: rituximab(anti B cell)

3. Disease condition:

- HIV infection especially when CD4 count dropping
- Proven increased susceptibility or morbidity/mortality e,g

Diffuse systemic disease e.g collagen diseases, diabetes, lymphoma, leukemia, metastatic cancer, frail elderly persons

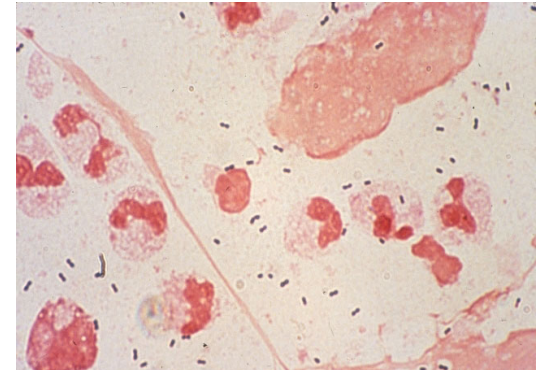
What are the risks for immunocompromised patients compared to the “normal population”?

Dramatic increased risk of influenza-related death in HIV patients

Deaths per 10, 000 persons	
Normal population	HIV (ages 25-54)
0.09-1.0	9.4-14.6

- Excess deaths 81-155 times higher in Dec- Jan than in general population of same age, compared with summer

- Early symptoms may be masked with monoclonal antibody therapy in rheumatoid arthritis.



Case reports of severe pneumococcal pneumonia in patients on tocilizumab (anti IL-6 receptor antibody)

- Increased invasive pneumococcal infections in solid organ transplant recipients.

Invasive pneumococcal infection
per 100,000 persons/year

SOT

General population

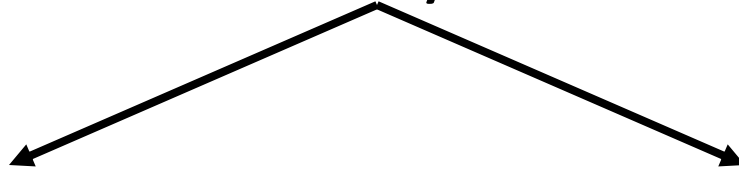
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11.5

(85% of strains were covered in the Pneumovax vaccine)

Human stem cell transplant patients

- Develop combined T- and B-cell immunodeficiency



- Lose immune memory Lose antibody



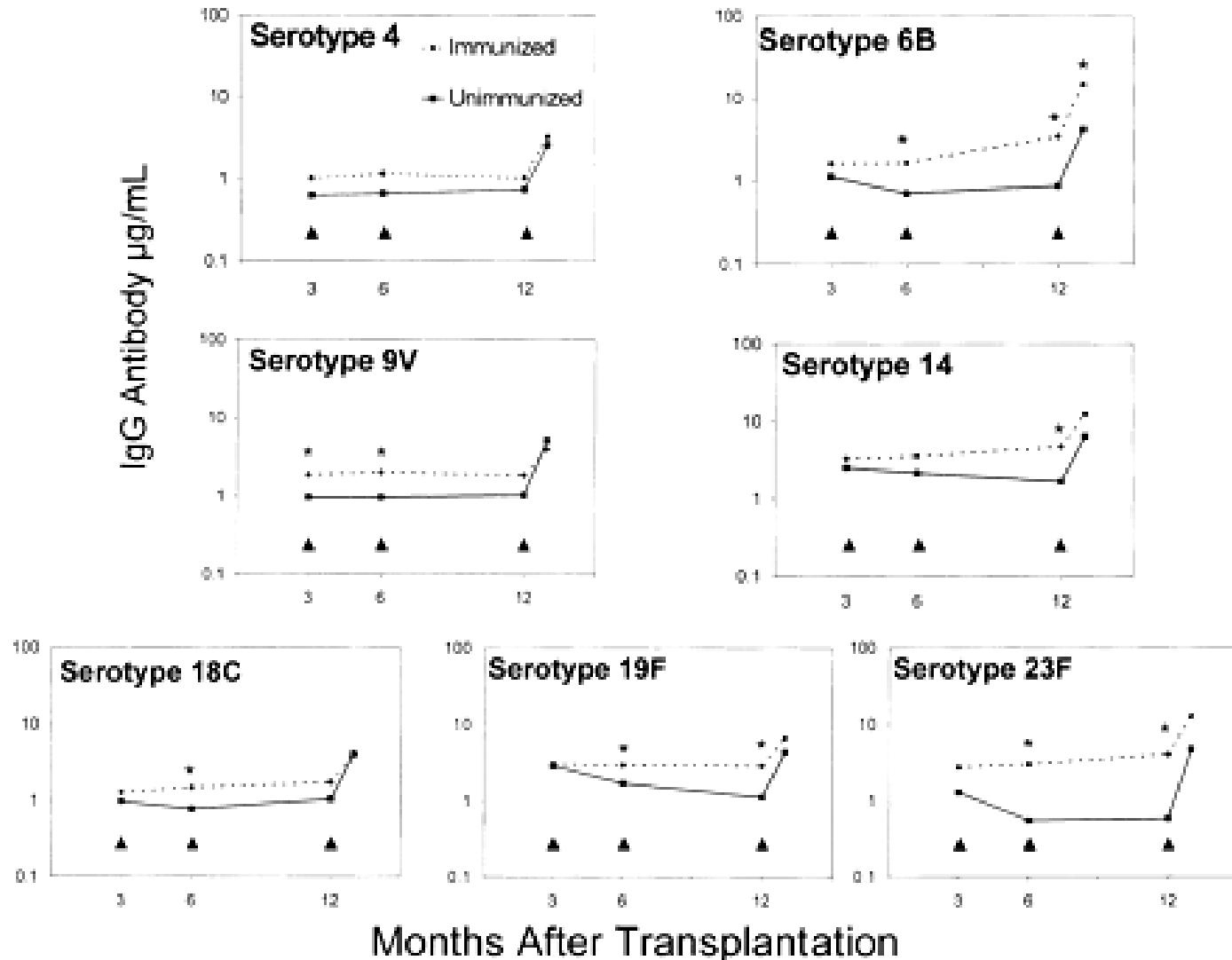
- Donor B-cells may contribute Ab temporarily
- Donor T-cells do not transfer immune memory well

- **Rule # 1.**
- **Fully immunize family members:**
 - DTaP, IPV,
 - Prevnar or pneumovax
 - Hib
 - Varicella (cover rash if occurs in vaccinee)
 - Yearly inactivated influenza, incl. children

BMT patients

- Immunize HSCT patients at 1 year, and then 2 years for live (MMR) vaccines (if stable and no GVHD)
- Fully immunize or boost **donor** BEFORE transplant (esp for B-cell function & antibody against *Streptococcus pneumoniae*)

Prevnar immunization of donors boosts adult allogeneic HSCT vaccine response.



**Centers for Disease Control and Prevention
recommendations for immunization in hematopoietic
stem cell transplant recipients**

Vaccine	Schedule
23-valent pneumococcal polysaccharide	12 and 24 months
<i>Haemophilus influenzae</i> type b conjugate	12, 14 and 24 months
Varicella zoster virus	Contraindicated
Influenza	Yearly lifelong resuming six months after hematopoietic stem cell transplant
Tetanus-diphtheria toxoid	12,14 and 24 months
Inactivated polio	12,14 and 24 months
Hepatitis B	12,14 and 24 months
Hepatitis A	Routine administration not recommended
Meningococcal	Routine administration not recommended
Measles, mumps, rubella	24 months if immunocompetent

Data from reference 4. Hematopoietic stem cell transplant (HSCT) recipients are considered immunocompetent at 24 months after HSCT if they are not on immunosuppressive therapy and do not have graft-versus-host-disease

Solid Organ Transplant

- Patients should be immunized when they are on the transplant list pre-transplant and are not severely immunosuppressed. If after transplantation, wait 6 months.
- Live vaccines such as varicella (if they have no measureable immunity), Zoster vaccine, MMR booster may be given 4 weeks before transplantation but not until 2 years after transplantation if immunosuppression is low.

- **Table 1. Vaccine Recommendations in HIV patients**
- **HIV-infected persons with CD4 counts <200 cells/ μL , history of an AIDS-defining illness, or clinical manifestations of symptomatic HIV are considered to have severe immunosuppression.**
- **Asymptomatic HIV-infected persons with CD4 counts of 200-500 cells/ μL are considered to have limited immune deficits.****
- **HIV-negative susceptible household contacts (especially children) of HIV-infected susceptible patients should be vaccinated against VZV, so that they will not transmit VZV to the HIV-infected patient. HIV-infected susceptible patients should limit their contact with recently vaccinated children or adults for 12-14 days after vaccination.**

Immunizing HIV Patients:

Pneumococcal (polysaccharide)

Recommended for all; consider revaccination every 5 years.

If CD4 count is <200 cells/ μ L, may be less effective; revaccinate when CD4 count increases in response to ART.

Hepatitis A Virus (HAV)

Recommended, for persons with chronic hepatitis C or hepatitis B, injection drug users, men who have sex with men, international travelers, and hemophiliacs. Consider for all, unless there is serologic evidence of previous disease. 2 doses (0, 6-12 months)

HIV Vaccine recommendations

- **Hepatitis B Virus (HBV)**
- Recommended, unless there is evidence of immunity (HBV surface Ab+) or active hepatitis B infection (HBV surface Ag+, or HBV core Ab+ and evidence of HBV activity).
- 3 doses (0, 1-2, 4-6 months)
- **Influenza (inactivated vaccine)**
- Recommended (yearly)
- Vaccination is most effective among persons with CD4 count >100 cells/ μ L and HIV RNA <30,000 copies/mL.
- In patients with advanced disease and low CD4 cell count, inactivated vaccine may not produce protective antibodies.
- Live, attenuated cold-adapted vaccine (LAIV, FluMist) is contraindicated in patients with HIV infection.

Immunization for HIV Patients

- **Tetanus-Diphtheria**
- **Recommended (booster is recommended every 10 years in adults; or, if injured)**

- **Measles, Mumps, Rubella (MMR)**
- **Recommended if indicated (eg, if contact with measles is likely through travel or other exposures). For live vaccine, use caution in those with low CD4 counts.**
- **Consider for all susceptible people who are not severely immunosuppressed.***
- **Contraindicated in severe immunosuppression.**

Varicella Zoster (VZV)**

Consider for asymptomatic patients with relatively high CD4 counts, if they have no history of chickenpox and no evidence of immunity or significant exposure.

Avoid in patients with advanced immunosuppression.

Avoid exposure to VZV, if possible. If someone without immunity to VZV is exposed to VZV, administer VZIG as soon as possible, at least within 96 hours.

Exposure to Varicella vaccinee OK if no rash.

Rheumatologic, autoimmune diseases –
Rheumatoid arthritis, lupus etc.

- < 20 mg prednisone for < 2 weeks – immunize as for normal host
- Most immunosuppression with high-dose steroids and DMARDs (especially Imuran) or Biologic DMARDs

- **Biologic DEMARDS:**

Anti-TNF antibody such as infliximab, and adalimumab may be less immunosuppressive¹ than rituximab² which acts to suppress antibody formation through depleting B-cells.

Abatacept costimulatory analogue has theoretically less affect on polysaccharide vaccines like Pneumovax.³

1. Kaine JL et al. J Rheumatol 2007;34:952-7
2. Gelinck LB. Ann Rheum Dis 2007;66:1402-3
3. Tay L et al. Arthrits Res Ther 2007;9:R38

Bottom Line

- All patients with autoimmune or rheumatologic diseases should be fully immunized with inactivated vaccines.
- Immunize household and close contacts
- Live vaccines:
- MMR booster as long as no severe immunosuppression e.g on maintenance steroids.
- Avoid live varicella or zoster vaccine.

Two important things for renal failure patients

- Only live vaccine contraindicated is live attenuated influenza vaccine (FluMist).
- Give special double dose formulation of Hep B vaccine, check HB_sAb after 4-6 weeks, and revaccinate if inadequate (<10 IU)

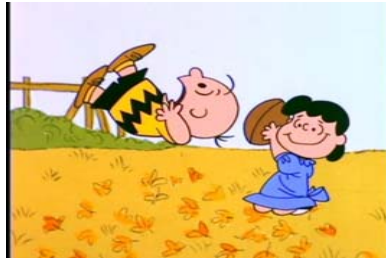
Inflammatory bowel disease

Immunize with:

- Influenza vaccine yearly
- Pneumovax every 3-5 years
- DT every 5-10 years

- Vaccinate when immunosuppression is least if possible.

Timing is important



- Immunize 4-8 weeks BEFORE initiation of potent immunosuppression.
- Influenza vaccine yearly
- Pneumovax every 3-5 years
- Hib vaccine every 5 years
- Meningococcal vaccine under specific conditions e.g travel, outbreak
- DT or DTaP every 5 years
- Hep A and B

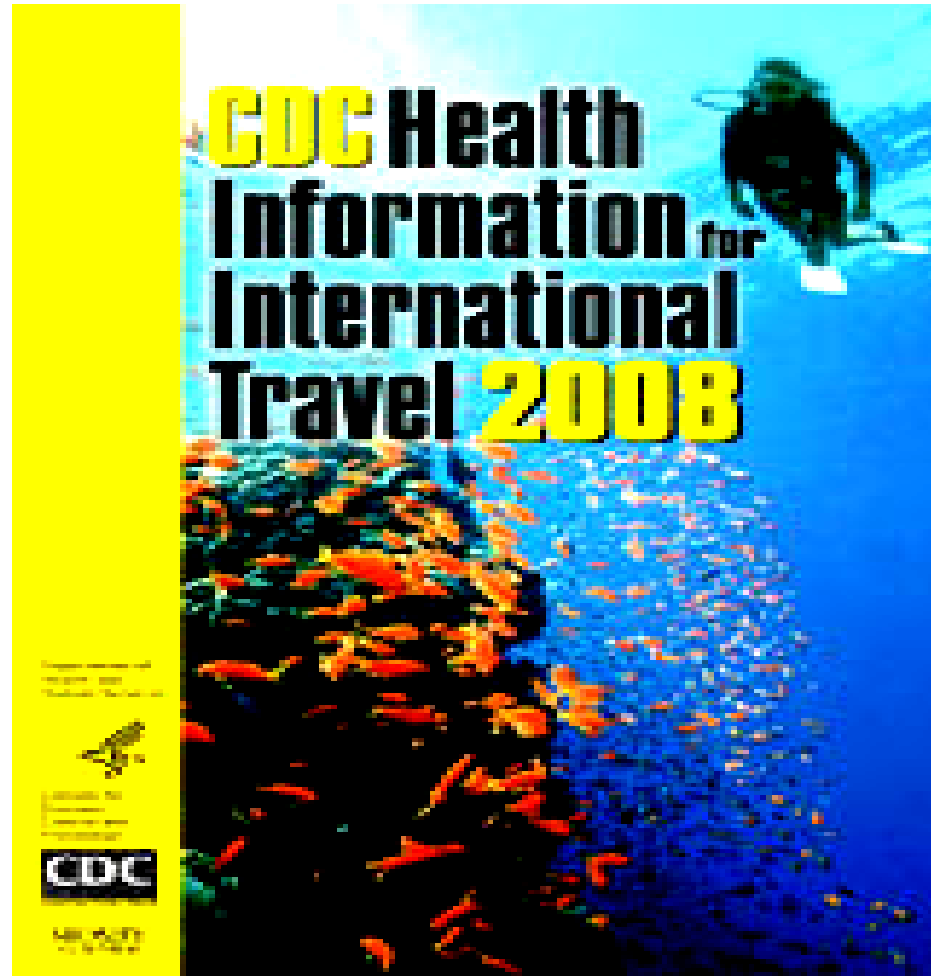
Splenectomized patients: trauma, hodgkins staging, sickle cell, ITP, thalassemia.

- If possible vaccinate BEFORE splenectomy
- Target polysaccharide capsule organisms:
- Streptococcus pneumoniae – Pneumovax
- Haemophilus influenzae – Hib
- Neisseria meningitidis – Menjugate, then Menactra in 2 weeks. Boost every 2-5 yrs
- One dose Pneumovax is sufficient, boost every 2-5 yrs

Pneumococcal DIC with purpura fulminans



Vaccinating the immunosuppressed traveller



Immunocompromised travellers

YES

NOT!

- DTaP
- Inactivated Polio
- Zostavax
- IM typhoid (Typhim Vi) (typhoid)
- Pneumovax
- Rabies (RabAvert)
- Japanese B encephalitis
- Meningococcal (both)
- Hib
- Influenza (inactivated)
- Cholera, Tourista ETEC (Dukoral)

OPV

MMR, Varivax or

Oral Vivotif Berna

Yellow fever

Live cholera (Mutachol)



Iomai ETEC patch

80% efficacy

Yellow fever only occurs in Africa and South and Central America

Figure 18. Yellow Fever Epidemiology in Africa at Country Level, 1950–2004

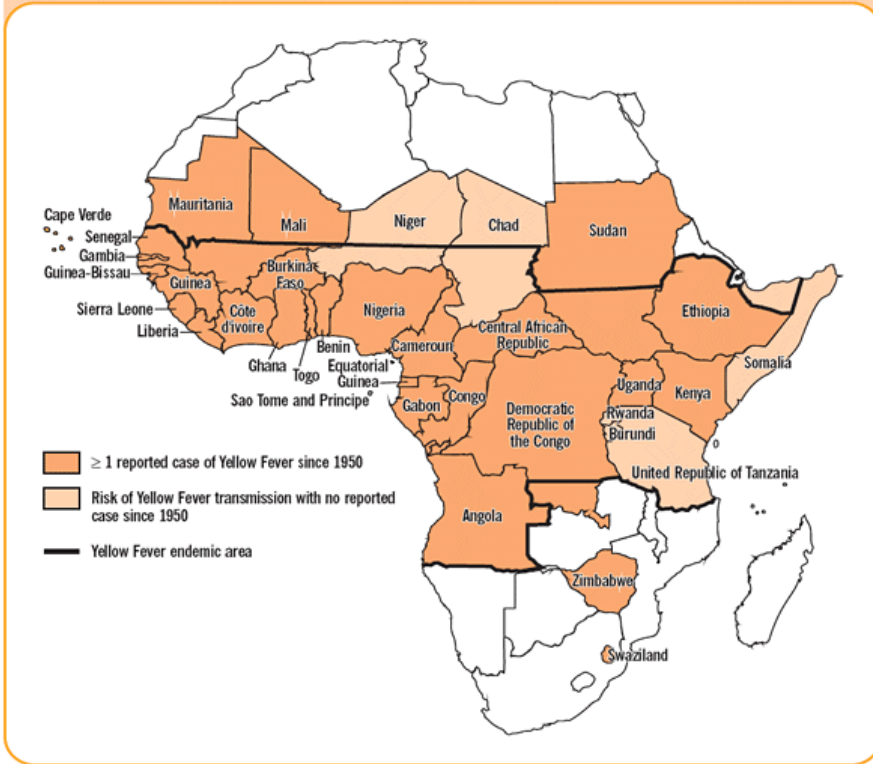


Figure 19. Yellow Fever Epidemiology in Central and South America at Country Level, 1950–2004



Why don't adults get vaccinated?



- 'Cause they're not scared enough!
- Vaccinated persons have lowered the risk
- They get bad advice about immunizations.

Post-exposure prophylaxis

- **Hep A** IM Ig 0.02 ml/kg within 14 days

- **Hep B** Percutaneous:

0.06 mlg/kg (5ml) IM Ig with Hep B vaccine within 24 hours

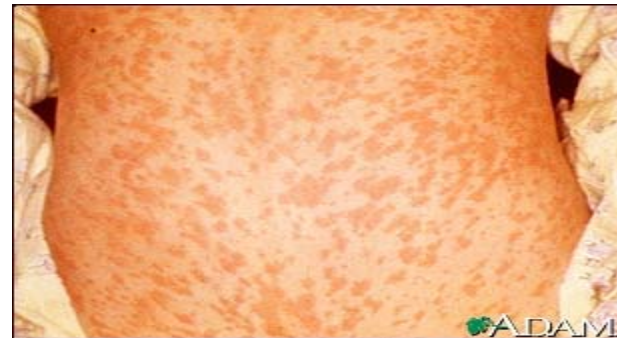


- Unprotected sexual contact:
0.06 mlg/kg or 5 ml within 14 days

Post-exposure prophylaxis

- **Influenza:**

Oseltamivir 75 mg po within 36 hours OR
Zanamivir 2 inhalations. Continue BID for 5
days together with all unvaccinated close
contacts. Treat the ill contact with NAI.



- **Measles:**

- IM Ig 0.5 ml/kg up to 15 ml within 6 days

Post-exposure prophylaxis

- **Varicella:**
- VZIG 125 U/10 Kg up to 625 U IM within 96 hrs
- **Meningococcal disease:**
- Ciprofloxacin 500 mg single dose; or Rifampin 600 mg daily for 2 days (**H.influenzae type b - 4 days**)

