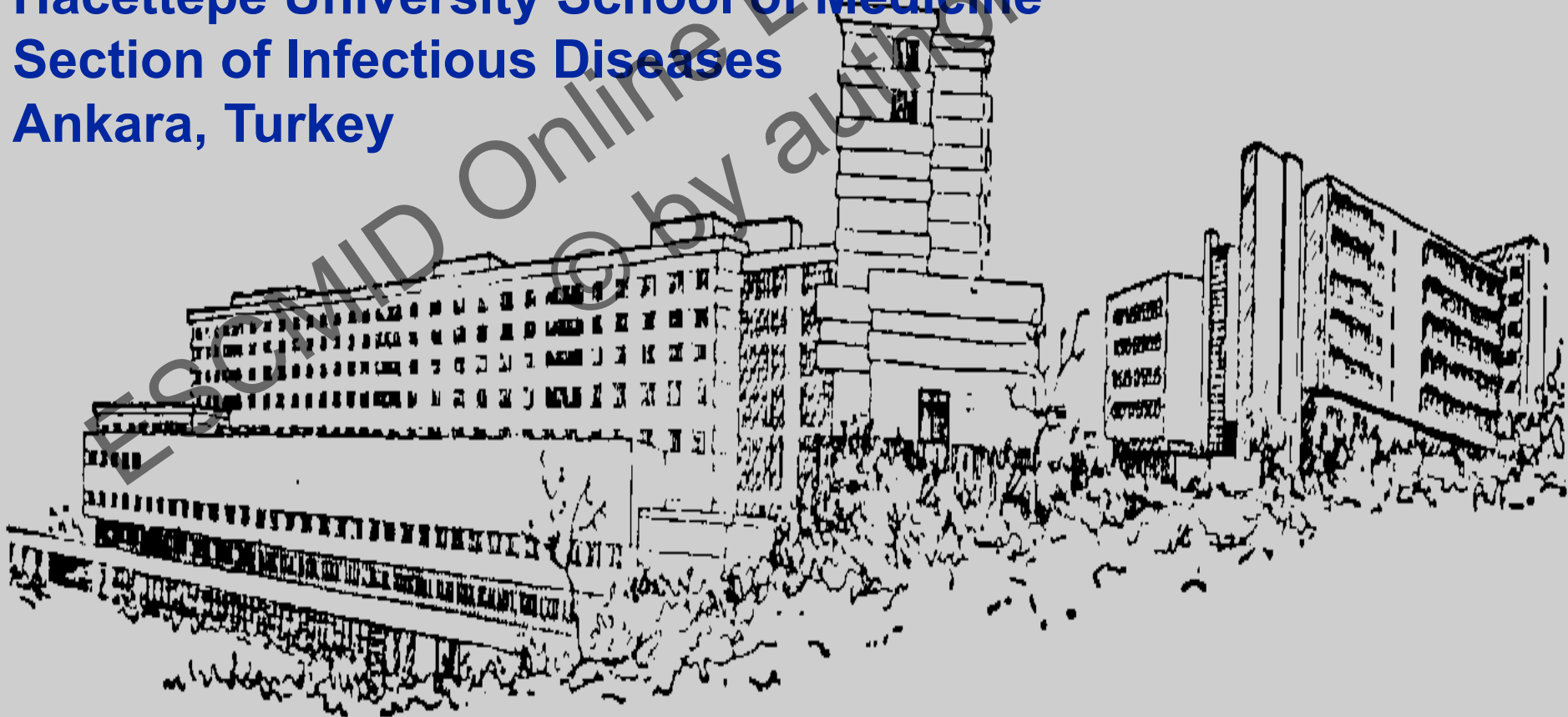


# Vaccines in Immunosuppressed Patients

**Dr. Murat Akova**

**Hacettepe University School of Medicine  
Section of Infectious Diseases  
Ankara, Turkey**



# The Extend of Immunosuppressive Patient Population

- An estimated 5-7% in the western society have immun-mediated diseases, treatable with biologicals
- In US, 2006
  - 173.339 living with solid organ transplant
  - 60% increase compared with 1996
- In UK, 1996
  - 409.000 using steroids
  - 93.000 recieving daily 7.5 mg prednisolone

# Types of Immunosuppression

- Immune-mediated inflammatory diseases (IMID)
- Patients using immunosuppressive or immunomodulatory drugs
- HIV/AIDS
- Diabetes mellitus
- Chronic renal failure
- End-stage liver disease
- Elderly
- Congenital immunodeficiency
- Splenectomy/asplenia
- Solid organ transplantation
- Hematopoietic stem cell transplantation

# IMID

- **Examples for diseases include**
  - Rheumatoid arthritis
  - Inflammatory bowel diseases
  - Multiple sclerosis
  - SLE
  - Psoriasis
- **Vaccination may lead lower protection rates**

# Vaccines for Patients with IMID

- **Some autoimmune reactions may be vaccine-related**
  - Myo- and pericarditis after variola vaccination
  - ITP after MMR vaccine
  - Guillain-Barré syndrome after 1976 swine flu vaccine

# Vaccines for Patients with IMID

- Inactivated or killed vaccines do not induce disease activity
- In SLE inactivated vaccines
  - Produce sufficient immunity
  - but reduced antibody levels for influenza and Hepatitis B
- All patients with IMID should receive
  - commonly recommended ones plus
  - influenza and pneumococcal vaccines

# Immuno-suppressive and Immuno-modulatory Drugs

- **Steroids**

- Inhibits IL-1, IL-2, IL-6, TNF and  $\gamma$ -IF
- Reduces T-cell proliferation and B-cell dependent antibody production
- Conflicting results with inactivated vaccines
  - 10-35 mg/d prednisolon may not affect PPV
  - But, may reduce immunity against influenza B
- Live vaccines should not be given to adults with  $>20$  mg/d prednisolone for  $>2$  weeks
  - At least 4 weeks after discontinuation

# Cytostatic Drugs

- All inhibit cell division
  - Affect T- and B-cell proliferation and inhibit cytokine proliferation
- MMF receivers, in only 10%, influenza vaccination stimulated 4-fold rise of antibody
  - Significantly lower than azathioprine receivers
- Evidence lacking of effectiveness of immunization in this group



# Other Drugs

- **Monoclonal antibodies**
  - Response to inactivated vaccines may be impaired up to one year
  - Live vaccines are contraindicated up to one year
- **Calcineurin inhibitors (cyclosporin, tacrolimus, sirolimus)**
  - DT booster effective in tacrolimus tx
  - Diminished response to influenza within 6 months of transplantation and with tacrolimus

# HIV/AIDS

## CD4 >200

- Influenza, yearly
- Tdap
- Pneumococcal vaccine
- Hep B series
- HPV series in those <26 years
- MMR, those born >1957 and not gotten vaccine
- Varicella, those born >1980 and not gotten 2 doses or have immunity

## CD4 <200

- Influenza, yearly
- Tdap
- Pneumococcal vaccine
- Hep B series
- HPV series in those <26 years

# Chronic Diseases

- **Diabetic patients may have decreased response rates to HBV vaccine**
- **HBV vaccine is routinely recommended in ESRD patients**
  - **Double dose for hemodialysis patients**
- **End stage liver disease**
  - **HBV, HAV, influenza and pneumococcal vaccines**

# Immunosenescens

- **Natural immunity**

- ↓ inflammatory response
- ↓ NK cells
- ↓ antigen uptake
- ↓ phagocytic and oxidative capacity

- **Adaptive immunity**

- **Diminished T-cell repertoire**
  - ↓ new T-cell production
  - ↓ effector T-cell
- **Low-affinity antibody response**
  - ↓ B-cell production

## Elderly

- **Decreased vaccine efficacy**
  - Influenza 17-53%
  - PPV 60%, PCV 13 may be more immunogenic
- **Live VZV vaccine ↓ incidence of herpes zoster by 51% and postherpetic neuralgia 67%**
  - Recommended for all >60 years in US and Canada

# Congenital Immunodeficiency

- Agammaglobulinemias sets in after maternal IgG disappears 6 months after birth
- The onset of common variable immunodeficiency is at 15-25 years
  - Ig is the treatment of choice
  - In general patients with congenital immunodeficiencies should not be given live or attenuated vaccines

# Splenectomy/Asplenia

- Severe infections caused by encapsulated bacteria
  - Mortality due to postsplenectomy sepsis 50-70%
- PPV23 and meningococcal vaccine should be given 2 weeks before splenectomy
- HiB recommended for unvaccinated in Europe

# Malignancies

- **No live vaccines**
- **Influenza vaccine 2 weeks before chemo or between cycles**
- **In CLL patients vaccination recommended in early stages and chemotherapy**



# Solid Organ Transplantation

- **Live vaccines during pretransplant period**
  - Except rubella for young women, others should be avoided posttransplant
- **Recommended**
  - Pneumococcal
  - Influenza
  - HAV and HBV
  - Td

# Hematopoietic Stem Cell Transplantation

- If not revaccinated, ab titers decline during 1-10 years posttransplant
- B-cell counts return normal by 3-12 months post-tx
  - If given rituximab, delays 6 months after last dose
- T-cell recovery
  - 6-9 months after tx in patients <18 years
  - 2 years in older with GVHD

# Vaccinations Recommended for Auto- and Allo- HCT Recipients

Vaccine	Time post-HCT (months)	No. of doses
PCV	3-6	3-4
TDaP	6-12	3
HiB	6-12	3
Meningococcal conjugate	6-12	1
Inactivated polio	6-12	3
rHBV	6-12	3
Inactivated influenza	4-6	1-2
MMR	24	1-2

# Vaccinations Optional for HCT Recipients

Vaccine	Recommendations
Hepatitis A	Follow recommendations for general population. Ig for PEP
Varicella (live)	Limited data
HPV	Follow recommendations for general population.
Yellow fever (live)	Limited data. Consider risk-benefit
Rabies	PEP is suitable with hyper Ig
Tick-borne encephalitis (TBE)	According to local policy. No data about timing after HCT
Japanese B encephalitis	Same as TBE

# Vaccinations not Recommended for HCT Recipients

Vaccine	Recommendations
BCG (live)	Contraindicated
Oral polio (live)	Inactivated alternative exist
Intranazal influenza (live)	No data
Cholera	No data
Typhoid oral (live)	No data
Typhoid (im)	No data
Rotavirus	Must be given before 12 weeks of age to be safe
Zoster (live)	No data

# Conclusions

- There is a large pool of immunosuppressed patients in the community
- In general
  - Lower antibody levels than normal can be achieved by vaccination
  - Delay immunization until immunosuppression is gone
  - Do not use live vaccines if possible

**Thank you....**

ESCMID Online Lecture Library  
© by author