To vaccinate or not?
Efficacy and safety of vaccines, as well as the increased need, in the older traveller

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The questions we will ask...
- Is there really a need for vaccination in older adults?
- What does an optimal immune response look like?
- What evidence is there for a decreased response to vaccines in older adults?
- What can be done to improve the efficacy of vaccines in older adults?

The goal of this talk is not to explicitly describe what happens with vaccines given to older adults, but to provide a framework for how all vaccines work across the lifespan of the patient and how to optimize them. The vaccines we have today will hopefully be obsolete in the future when they are replaced by better versions or the diseases are eradicated.

Financial Disclosures
- Mark P. Walberg, Pharm.D., PhD, CTH discloses the following relationships:
  - Previously employed as a paid speaker for Merck Vaccines
  - Currently retained as a paid legal consultant for Merck Vaccines
  - Currently employed by GlaxoSmithKline

This conflict has been resolved per ACPE best practices.

Optimal Immune Response
- Production of high concentrations of high-affinity IgG
- Prevention of infections
- At higher concentrations, may diffuse to surfaces and protect like IgA
- Easiest immune response to measure
- Formation of memory B and T cells
- Easiest immune response to measure
- Upon stimulation will elicit greater antibody production at a faster rate than initial exposure
- More difficult to measure memory formation directly

US Hepatitis A and B Immu...
Optimal Immune Response

1. Injected polysaccharide is recognized by germ-line B cells
2. B cells proliferate
3. Differentiation into plasma cells
4. Production of antibodies and only antibodies remain months or years after stimulation

Key limitation: no immunological memory, therefore no ability to boost immunity at a later time.

Polysaccharides are used as a defense mechanism by bacteria to evade immune recognition, e.g., S. pneumoniae & N. meningitides.

The T cell Dependent Germinal Center/Follicular Reaction
5. Injected protein is phagocytosed and presented to both germ-line B cells and T cells
6. B and T cell pair moves to lymph node and initiates a germinal center reaction
7. B cells undergo hypermutation and affinity maturation and form plasma cells of a single lineage
8. Plasma cells produce high-affinity antibodies and a population of memory T cells is created. To become memory T cells, they have to be reactivated.

Key limitation: only works with protein antigens, may take multiple doses, giving higher boost immune effect, takes time to fully develop memory cells (months)

Figure from Chapter 2 of Plotkin SA, Orenstein WA, Offit PA, eds. Vaccines. 7th ed. Elsevier Saunders; 2018: 1691 pgs.

Vaccine Response in Older Adults


Proposed mechanisms for lower immune responses in older adults:
- Decreased activity or development of antigen-presenting cells
- Decreases in naïve T cells
- Poorer IgG production from germinal centers
- Decreased plasma cell formation and survival

Can we improve response to vaccines?
- Quality of antigen
- Quantity of antigen
- Uptake of antigen

Antigen Matters...


Conjugation helps, but not entirely...


More frequent dosing may or may not help...

Influenza:
Young B, et al. Semiannual Versus Annual Influenza Vaccination in Older Adults in the Tropics: An Observer-blind, Active-comparator–controlled, Randomized Superiority Trial. CID 2018; ciy836. DOI: https://doi.org/10.1093/cid/ciy836

While antibody titers weren’t appreciably different, semiannual administration significantly decreased ARI and ILI.

Always remember when looking at influenza vaccines that when you see one year, you have only seen one year... It is very difficult to extrapolate to future seasons!
Does a higher dose help? Sometimes…


Figure 1. Relative Vaccine Efficacy in Various Population Subgroups. The relative risk is the percentage of participants with documented flu in the RIV4 group (the RIV4 attack rate) divided by the percentage of participants with documented flu in the IIV4 group (the IIV4 attack rate). The relative vaccine efficacy was calculated as [100 × (1 – relative risk)]. RT-PCR denotes reverse transcription polymerase chain reaction. The squares represent the point estimate of the treatment effect.

Adjuvants may also be beneficial...


Figure 1. Results for heterologous strains in 4 first-dose randomized controlled trials (full analysis set [FAS]). Differences in percentage of subjects with seroconversion (SC).

Can we improve response to vaccines?

• Quality of antigen
  • Improvements are possible (conjugate versus pure polysaccharides), but some antigens are just better than others.

• Quantity of antigen
  • Larger doses of antigen, but not more frequent administration, may be beneficial.

• Uptake of antigen
  • Adjuvants appear to increase immune response and may be beneficial.

Why memory matters...


Figure 1. Kaplan-Meier estimates of the cumulative risk of herpes zoster (HZ) by HZ vaccination status.

Why memory matters...


Figure 1. Geometric mean titre by age group as measured by the haemagglutination inhibition and microneutralisation assays in baseline serum samples obtained in 2008. Error bars represent 95% CI.
Why memory matters...


Figure 1. Neutralizing Antibody Responses to the 2009 Pandemic H1N1 Virus among Serum Donors, According to Birth Decade (1880–2000).

Serum samples that were collected in 1971 and between 2002 and 2009 were tested by a microneutralization assay. The proportion of subjects with neutralizing antibody titers of 40, 80, 160, 320, and ≥640 are plotted on the left ordinate, according to the birth decade of the serum donor. The cumulative geometric mean titer (GMT) for all subjects in a birth decade and in all preceding birth decades is plotted on the right ordinate and is shown with black circles.

Childhood vaccinations may be the answer...

Schedule available from https://www.cdc.gov/vaccines/schedules/hcp/imz/child-adolescent.html

Schedule available from https://www.cdc.gov/vaccines/schedules/hcp/imz/adult.html

Thank you for attending... and remember...

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