Cotrimoxazole prophylaxis (CPT), INH prophylaxis (IPT) & immunisation practice

Rudzani Muloiwa, Department of Paediatrics & Child Health, Groote Schuur Hospital, University of Cape Town, South Africa

Paediatric HIV course: 13th September 2016
Principles of prophylactic therapy

a) Condition being prevented must have a significant impact

b) The risk of condition arising must be significant

c) Prophylaxis must be effective

d) Benefits must outweigh potential side effects

e) Review of changes in risks and benefits must be continuous
Indications of CPT in Children & Adolescents

- HIV-exposed infants <1 year - start at 4-6 weeks
- HIV-positive infants <1 year regardless of CD4 count
- HIV-positive children 1-5 years with WHO stage 2, 3 or 4; CD4 <25% or <500.
- If previous PCP: stop at 5 years old
- HIV-positive children >5 years with WHO stage 3 or 4 or CD4 <200. Discontinue CPT if CD4 >200 on two consecutive occasions 3-6 months apart.
- Co-infection with TB
Contraindications for CPT

- Known or suspected hypersensitivity to Sulphonamides/Trimethoprim
- Common side-effects: Maculopapular rash/hypersensitivity reaction
- Can be mild or severe Stevens Johnson syndrome
- Dapsone can be used in patients with mild reactions

NB. Refer to experienced clinician for management if SJS or contraindicated patient need treatment for PCP
Indications IPT in Children & Adolescents

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Why focus on vaccination of HIV+ population?

A) Introduction

- Advancement & availability of HIV treatment has dramatically increased the life expectancy of HIV-infected persons.

- As a result, the proportion of HIV-infected persons is increasing in South Africa (SA) as well as the rest of the world.

- For example in SA, from 2002 to 2014, the HIV/AIDS related deaths has decreased from 44% to 31%.

The increase in the proportion of HIV+ population is important to the vaccination programs!
Why focus on vaccination of HIV+ population?

A) Introduction…ctn’ed

-In SA, PMTCT program has been very successful (to almost elimination) in preventing perinatal HIV infection

-Therefore, majority of the persons living with HIV-infection are more likely to be adolescents/adults.

-There are no national adolescents’ and adults’ vaccination programs in SA.
Immune responses to vaccination in HIV+ population

**IMMUNE RESPONSES** - There are reports showing that HIV infection could result to:

a) attenuated vaccine-induced immunity
b) reduced anamnestic responses to vaccination
c) accelerated loss of vaccine-induced immunity

**SAFETY** - Also, some reports show reduced safety profile of some commonly used vaccines (especially live) when administered to HIV+ persons.

*If the above holds true, then, despite improved care & treatment, the increasing numbers of HIV+ population may result to reduced herd immunity and outbreaks of VPDs in the future*
B) What is known about vaccination of HIV+ population?

Long-term Immune Responses to Vaccination in HIV-Infected Patients: A Systematic Review and Meta-Analysis

Solen Kernéis, Odile Launay, Théophile Trébuchon, Frédéric Batteux, Thomas Hanslik, and Pierre-Yves Boëlle

Vaccine-induced antibodies may wane more quickly in persons living with human immunodeficiency virus (HIV) than in healthy individuals. We reviewed the literature on vaccines routinely recommended in HIV-infected patients to estimate how seroprotection decreases over time in those who initially responded to immunization. For each study retrieved from the literature, the decrease of seroprotection was modeled with a log-normal generalized linear model, and data were pooled in a meta-analysis to provide estimates of seroprotection 2 and 5 years after the last vaccine administration. Our analyses confirmed that the duration of seroprotection was shorter in HIV-infected patients and that with current guidelines, a substantial proportion of patients would have lost protective antibodies before a booster was proposed. We therefore discuss the implications for the monitoring of antibody levels and timing of revaccination in these patients.

Keywords. vaccination; HIV; meta-analysis.
Concerns

• The rate of adverse events may be higher in HIV positive recipients of vaccines.

• The administration of live attenuated viral or bacterial vaccines is not generally recommended in individuals with overt immune deficiency.

• May cause activation and proliferation of T cells, cytokine release, and an increase in HIV-1 replication.

• Plasma viral load generally returns to baseline within 6–8 weeks but little is known about the long-term consequences of these repeated bursts of “transient viraemia”.

• If vaccination stimulates the immune system sufficiently to increase viral replication, then illness due to the same pathogen would probably induce a more substantial effect on viral replication and CD4+ T-cell depletion.
Vaccination in HIV infected persons
Some general observations

a) Risks may be higher than in the general population

b) Benefits may also be higher than in the general population

c) Timing is crucial in maximizing benefits while minimizing risk

d) The risk of a vaccine preventable condition arising must be balanced against potential adverse effects of vaccine
Goals in immunisation

• To prevent infection. E.g. Polio

• To prevent disease
  – i.e. Infection still takes place but the disease itself is prevented by vaccine. E.g. tetanus

• To prevent severe forms of disease
  – Vaccination does not prevent all forms of the disease but severity of disease is better. E.g TB
Types of active immunisation

- Alive
  - e.g. polio (oral), BCG, measles, mumps, rubella

- Dead
  - e.g. pertussis

- Toxoids
  - inactivated yet antigenic toxin (e.g. tetanus, diphtheria, pertussis)

- Polysaccharide vaccines
  - e.g. pneumococcal vaccine

- Conjugate vaccines
  - capsular carbohydrate linked to protein to make it immunogenic (e.g. H. influenza)
Live vaccines

- May be destroyed by improper handling (e.g. break in ‘cold chain’)
- Potentially dangerous
  - during fetal development
  - if immunocompromised
- Antibodies/blood transfusion likely to destroy vaccine
RSA Immunisation Schedule  
*from April 2009*

<table>
<thead>
<tr>
<th>Age</th>
<th>Vaccines</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth</td>
<td>TOPV(0), BCG</td>
</tr>
<tr>
<td>6 weeks</td>
<td>TOPV(1), DaPT-IPV/Hib(1), HBV(1), RV(1), PCV1(1)</td>
</tr>
<tr>
<td>10 weeks</td>
<td>DaPT-IPV/Hib(2), HBV(2)</td>
</tr>
<tr>
<td>14 weeks</td>
<td>DaPT-IPV/Hib(3), HBV(3), RV(2), PCV13(2)</td>
</tr>
<tr>
<td>9 months</td>
<td>Measles(1), PCV13(3)</td>
</tr>
<tr>
<td>18 months</td>
<td>Measles(2), DaPT-IPV/Hib(4)</td>
</tr>
<tr>
<td>6 years</td>
<td>Td</td>
</tr>
<tr>
<td>12 years</td>
<td>Td</td>
</tr>
</tbody>
</table>

OPV=oral polio vaccine  
IPV=inactivated polio vaccine  
BCG=Bacillus Calmette Guerin (against TB)  
DaPT=diphtheria, acellular pertussis, tetanus  
HBV=hepatitis B virus  
Hib=Haemophilus influenzae type b  
RV=rotavirus  
PCV=Pneumococcal conjugate vaccine (Prevnar 13)  
Td = tetanus, reduced strength diphtheria
RSA Immunisation Schedule
(from December 2015)

Birth
TOPV(0), BCG
6 weeks
TOPV(1), DaPT-IPV/Hib(1)/ HBV(1), RV(1), PCV1(1)
10 weeks
DaPT-IPV/Hib/ HBV(2)
14 weeks
DaPT-IPV/Hib/ HBV(3), RV(2), PCV13(2)
6 months
Measles
9 months
Measles(1), PCV13(3)
12 months
Measles
18 months
Measles(2), IPV/DaPT/Hib(4)
6 years
Td
9+ years
HPV
12 years
Td

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PCV=Pneumococcal conjugate vaccine (Prevnar 13)
Td (tetanus, reduced strength diphtheria)
HPV=Human papillomavirus
Other currently available vaccines

- Mumps
- Rubella
- Meningococcal
- Influenza
- Hepatitis A
- Chicken pox
- Cholera
- Typhoid
- Rabies
- Japanese encephalitis
- Anthrax
- Small pox
- Tick-borne encephalitis
- Yellow Fever
Vaccines that provide herd protection

- Inactivated poliovirus
- Diphtheria
- Pertussis
- Measles, mumps, and rubella
- Varicella
- Meningococcal
- Hepatitis A
- Hepatitis B
- Parenteral typhoid
- BCG
- Pneumococcal

These will indirectly protect an unimmunized HIV infected individual in a highly vaccinated population
Vaccines that do not provide herd protection or immunity

• Tetanus
• Rabies
• Japanese encephalitis

Do not indirectly benefit the HIV-infected individual
Safe to use inactivated vaccines

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Indication</th>
<th>Common use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anthrax</td>
<td>RS</td>
<td>Occupational</td>
</tr>
<tr>
<td>Cholera (WC/rBS)</td>
<td>RS</td>
<td>Travel</td>
</tr>
<tr>
<td>Hepatitis A</td>
<td>RS</td>
<td>Risk groups</td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>R</td>
<td>Risk groups</td>
</tr>
<tr>
<td><em>Haemophilus influenzae</em></td>
<td>RS</td>
<td>Risk groups</td>
</tr>
<tr>
<td>Influenza-parenteral</td>
<td>R</td>
<td>Indications are strengthened in the presence of additional risk factors</td>
</tr>
<tr>
<td>Japanese encephalitis</td>
<td>RS</td>
<td>Travel</td>
</tr>
<tr>
<td>Meningococcus (MenC)</td>
<td>RS</td>
<td>Risk groups</td>
</tr>
<tr>
<td>Meningococcus (ACWY)</td>
<td>RS</td>
<td>Travel</td>
</tr>
<tr>
<td>Pneumococcus (PPV23)</td>
<td>R</td>
<td>Indications are strengthened in the presence of additional risk factors</td>
</tr>
<tr>
<td>Rabies</td>
<td>RS</td>
<td>Travel</td>
</tr>
<tr>
<td>Tetanus–diphtheria-parenteral poliomyelitis (Td/IPV)</td>
<td>RS</td>
<td>Uncertain vaccination status or travel</td>
</tr>
<tr>
<td>Tick-borne encephalitis</td>
<td>RS</td>
<td>Travel</td>
</tr>
<tr>
<td>Typhoid (ViCPS)</td>
<td>RS</td>
<td>Travel</td>
</tr>
</tbody>
</table>

R, recommended in all; RS, recommended in selected groups.
Live vaccines safe to use if CD4 count > 200

Vaccine

Measles, mumps, rubella (MMR)
Varicella
Yellow fever
### Contraindicated live vaccines - irrespective of CD4 counts

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cholera (CVD103-HgR)</td>
<td>Also contraindicated in close contacts</td>
</tr>
<tr>
<td>Influenza (intranasal)</td>
<td>Also contraindicated in close contacts</td>
</tr>
<tr>
<td>Oral poliomyelitis (OPV)</td>
<td></td>
</tr>
<tr>
<td>Typhoid (Ty21a)</td>
<td></td>
</tr>
<tr>
<td>Tuberculosis (BCG)</td>
<td></td>
</tr>
<tr>
<td>Smallpox (Vaccinia)</td>
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</tbody>
</table>
Unownns

- What should a recommended schedule look like in HIV?
- Should this differ from the regular schedule?
- Is there a need to revaccinate? Which subjects? Which vaccines?
- Does the timing of ARV initiation make a significant impact?
- How does this differ from vaccine to vaccine?
- Should vaccination be individualised as opposed to being based on a standardised schedule
Conclusions

- IPT and CPT make have a huge impact on the management of HIV infected children
- Need to balance benefit and SE of prophylaxis
- HIV infected individual show higher susceptibility to infection but exhibit impaired responses to vaccines
- Only few absolute contraindications to vaccination in HIV+ individuals, pertaining mainly to live vaccines
- HIV infected subjects likely to derive great benefit from use of both EPI and non EPI vaccines
- A lot remains unknown about the best use of vaccines in HIV infected individuals