Study day
« Immunization of at-risk population »
: Immunization of the HIV-Infected Adults

Philippe Léonard
CHU Sart Tilman
23/11/2012

The good questions

- Are HIV-infected people at higher risk of infection?
- Impact of the vaccination on the HIV infection?
- Are vaccines dangerous?
- Does vaccines work in HIV-infected people? Which one and how to do?
The good questions

- Are HIV-infected people at higher risk of infection?
- Impact of the vaccination on the HIV infection?
- Are vaccines dangerous?
- Does vaccines work in HIV-infected people? Which one and how to do?

Higher risk of infection in HIV?

- **Influenza** *(Radwan, Clin Infect Dis 2000;31:604-6; Lin, Arch Int Med 2001;161,441-6)*
  - HIV people are highly susceptible to the infection
  - Replication of influenza continue for weeks to month
  - Influenza infection may last longer
  - Increased risk for complication and death

  - Higher morbidity and mortality
  - Higher risk of pneumonia (X 6 to 8) and of invasive pneumococcal disease (X 40)
    - Risk factors: comorbidities, alcohol, anterior hospitalisation, CD4<100/mm³, smoking
Incidence of first-time hospitalization to treat pneumonia in Denmark among individuals with and without HIV infection, 1995–2007


Higher risk of infection in HIV?

  - Patients with chronic liver disease and chronic infection with hepatitis B or hepatitis C are at risk of severe complications
  - HAV infection does not appear to be worse in HIV, but viremia may be prolonged (median of 53 days, but until 256 days!), with risk of spread and epidemic in MSM

- **Hepatitis B** (Thio, Lancet 2002; 360:1921-6; Koropnicki AIDS 2005; 19: 693-697; Alter, J Hepatol 2006, 44 (1S); S6-9)
  - Higher morbidity and mortality among HIV-infected people
    - Quick evolution to cirrhosis and end stage disease
    - Reactivation of latent disease
    - Hepatocarcinoma more aggressive and at younger age
  - Complications of viral hepatitis are among leading causes of death
  - Higher prevalence of chronic HBV in HIV infected people (6-15%)
  - HAART hepatic toxicity more frequent
Liver related mortality in patients coinfected HIV/HBV

Thio CL et al., 9th CROI, Seattle 2002, #656

Higher risk of infection in HIV?

  - HIV childrens have more *H. i.* but due to non typable strains
  - Severe infection, high mortality

- **Meningococcus** (Cohen, AIDS 2010;24:1231-42; Andrade, Braz J Infect Dis 2011;15:173-80)
  - Mainly serogroup B ans C
  - Increased incidence of meningococcal disease in HIV-infected individuals
  - Higher fatality
  - Fatal cases due to non hyper-virulent clonal complex
The Effect of Human Immunodeficiency Virus Infection on the Distribution and Outcome of Pneumonia in Intensive Care Units

KELLY J. TUCKER, MD, San Francisco; BETTE ANTON, MD, Denver; and HARVEY J. TUCKER, MD, San Francisco, California

**TABLE 1. Cause of Pneumonia and Outcome**

<table>
<thead>
<tr>
<th>Organism</th>
<th>Patients HIV Positive, No. (%)</th>
<th>Patients Hospitalized, No. (%)</th>
<th>Mortality, No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pneumocystis carinii</td>
<td>74 (28)</td>
<td>74 (100)</td>
<td>26 (32)</td>
</tr>
<tr>
<td>Streptococcus pneumonia</td>
<td>35 (13)</td>
<td>17 (49)</td>
<td>18 (51)</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>30 (11)</td>
<td>2 (7)</td>
<td>12 (40)</td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>20 (8)</td>
<td>0 (0)</td>
<td>10 (50)</td>
</tr>
<tr>
<td>Hemophilus influenzae</td>
<td>12 (4)</td>
<td>2 (17)</td>
<td>2 (17)</td>
</tr>
<tr>
<td>Viral</td>
<td>11 (4)</td>
<td>3 (27)</td>
<td>2 (18)</td>
</tr>
<tr>
<td>Indeterminate</td>
<td>56 (21)</td>
<td>6 (11)</td>
<td>18 (32)</td>
</tr>
<tr>
<td>Other</td>
<td>28 (10)</td>
<td>0 (0)</td>
<td>4 (14)</td>
</tr>
<tr>
<td>Total</td>
<td>266 (100)</td>
<td>104 (39)</td>
<td>92 (34)</td>
</tr>
</tbody>
</table>

*Percentages add up to less or more than 100% because of rounding off.

Tableau 6. N. meningitidis : répartition par groupe d’âge et par sérogroupe (N : 2011)

<table>
<thead>
<tr>
<th>Groupe d’âge</th>
<th>B</th>
<th>C</th>
<th>X</th>
<th>Y</th>
<th>W135</th>
<th>Non Groupable</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 1 mois</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>1-11 mois</td>
<td>15</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>1-4 ans</td>
<td>23</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>5-9 ans</td>
<td>4</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>10-14 ans</td>
<td>4</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>15-19 ans</td>
<td>12</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>20-24 ans</td>
<td>6</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>25-44 ans</td>
<td>8</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>45-64 ans</td>
<td>9</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>≥ 65 ans</td>
<td>4</td>
<td>8</td>
<td>0</td>
<td>6</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>85</td>
<td>15</td>
<td>0</td>
<td>9</td>
<td>1</td>
<td>2</td>
</tr>
</tbody>
</table>

Tableau 2. N. meningitidis : répartition selon la nature de l’infection (N : 2011)

- Meningite : 35
- Meningite + Septicémie : 25
- Septicémie : 34
- Bactériémie : 3
- Autres : 15
- Total : 112

8 décès consécutifs à ces infections ont été signalés (case fatality rate = CFR = 7,14%).

Centre National de Référence des Neisseria Meningitidis

2011 RAPPORT ANNUEL
Higher risk of infection in HIV?

- **Papillomavirus**
  - 130 strains (and more?), more than 30 sexually transmitted
  - Oncogenic virus (20 strains), causing intraepithelial neoplasia and squamous cell carcinoma, mainly HPV 16 and HPV 18
  - Squamous cervical cancer (second most common female cancer)
    - Higher prevalence of HPV in HIV women without cancer
    - 20% of HIV women will develop cervical squamous intraepithelial lesion within 3 years
    - AIDS-defining malignancy
    - Younger women, higher progression rates, more advanced disease, higher recurrence rates and overall poor prognosis
    - Greater diversity of HPV types, greater prevalence of multiple HPV types and greater preponderance of types other than HPV-16 and HPV-18
  - Anal cancer
    - Incidence of anal cancer increasing despite HAART
    - The standardized incidence ratio (SIR) of anal carcinoma in people with HIV/AIDS is between 19 and 50
    - Anal intraepithelial cancer of HIV MSM: increased risk if HPV 16, HPV 18 and Nadir CD4
  - Vulvar, vaginal, penis and oropharynx cancer

- **Measles**
  - The case fatality rate for severe measles was about 40% for HIV-infected patients

- **Varicella-Zoster virus**
  - Severe disease with high risk for developing varicella pneumonia and death
  - Severe and debilitating zoster

- **Typhoid fever**
  - Recurrent *S. non-typhi* septicemia = AIDS
  - Significantly increased risk for infection with *S. typhi* and *S. paratyphi*

- **Poliomyelitis**
  - AIDS is a risk factor for post-polio syndrome
  - Far from the year 2000 objectives of WHO
The good questions

- Are HIV-infected people at higher risk of infection?
- **Impact of the vaccination on the HIV infection?**
- Are vaccines dangerous?
- Does vaccines work in HIV-infected people? Which one and how to do?

Impact of vaccination on HIV disease?

- T-lymphocyte proliferation induced by vaccination can transiently increase plasma HIV-1 RNA levels, but with apparently no effect on HIV-1 disease progression
  - Tetanus, Influenza, Pneumococcus and Hepatitis B
- Higher stimulation of HIV by these natural diseases!

But impact on clinical studies

- Avoid measuring Viral Load some weeks after vaccination ….
- … what about clinical studies?
  - Inclusion criteria
  - Interpretation of results

The good questions

- Are HIV-infected people at higher risk of infection?
- Impact of the vaccination on the HIV infection?
- Are vaccine dangerous?
- Does vaccines works in HIV-infected people? Which one and how to do?
Safety of vaccine

- Concern live attenuated vaccine
- Risk of vaccinal disease
  - High: contraindication!
    - BCG (Mansoor, J Infect Dis 2009; 199: 982-90)
    - OPV
  - Depending on immunity (avoid if CD4<200/mm$^3$)
    - MMR
    - Varicella
    - Oral Typhoid Fever Vaccine
    - Zoster
    - Yellow fever

The good questions

- Are HIV-infected people at higher risk of infection?
- Impact of the vaccination on the HIV infection?
- Are vaccine dangerous?
- Does vaccines works in HIV-infected people? Which one and how to do?
Some requirements

- Immune humoral and cellular responses are inversely correlated with CD4 count
- Magnitude of Ab response to vaccination is often inversely correlated with CD4
- Vaccination generally not recommended if CD4<100/mm³
- Other factors
  - Malnutrition
  - Intercurrent infections
  - Comorbidities
- Faster antibody decline in HIV after immunization

Improved immunity

- HAART effectiveness
  - Increase in CD4 and B cells counts, (including naive and memory cells)
    - For humoral and cellular immunity to T-cell dependent and T-cell independent immunogens
  - Improvement of magnitude and longevity of immune responses to natural infection and vaccinations
  - Growing evidence that suppressed HIV RNA load improves response to vaccination (Hepatitis A, Hepatitis B, Japanese Encephalitis, Varicella, Influenza, Pneumococcus, Yellow Fever) and this is generally achieved within 6 month of starting HAART
Some (many) questions remains…

- Repeat routine vaccination after starting HAART in adults who received routine immunizations in childhood? But immunity to vaccine received before immunodepression is usually maintained.
- How long wait after HAART introduction?
  - 3 to 6 month?
- Wait 3 month after immune reconstitution (CDC, Travel Yellow Book, 2012)
- If immunized while CD4 < 200/mm³, revaccine at least 3 month after immune reconstitution?
- Another vaccinal schema?

---

2.3. Adultes et adolescents ≥ 16 ans

<table>
<thead>
<tr>
<th>MALADIES (commissinées)</th>
<th>VACCINS INACTIVES</th>
<th>VACCINS VIVANTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV/CD4 &lt; 200/mm³</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HIV/CD4 200-500/mm³</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### LEGENDE

- **C:** vivement conseillé, vu le risque complémentaire sous forme de sensibilité accrue et/ou de gravité accrue et/ou de risque accru de complications.
- **R:** à envisager en cas de risque épidémiologique ou personnel.
- **NA:** non applicable.
- **S:** Indication standard de la vaccination car il s'agit de vaccinations de routine faisant partie du schéma vaccinal de base valable pour toute la population.
- **X:** déconseillé en raison des contre-indications.
Flu vaccination

- Lower antibodies response in HIV
  - (Zanetti, Vaccine 2002; 20: B29-32)
- Better flu protection in HIV, compared to placebo or no vaccination
  - (Beck, J Infect Dis 2012; 206: 1250-9)
- Immunogenicity is not improved by increased antigen dose or by booster dosing
  - (Cooper PlosOne 2011; 25(6):3 e17788)
- Better Ab response if CD4>200/mm³
  - (Knoon, AIDS 1998; 12(7): F217-23)
- Most guideline recommand flu vaccination, irrespective of CD4 count

Flu vaccination

- Viral antigens: hemaglutinin and neuraminidasis of 3 strains
- Yearly vaccination
  - Eggs allergy
    - gentamycin, polymyxin B, neomycin
- α-RIX®, VAXIGRIP®, INTANZA®: fragmented inactivated virus
- INFLUVAC S ®: Surface antigens
- INFLEXAL V®: Virosomal, surface antigens
Pandemic influenza

- Better response to pandemic ASO3-adjuvented AH1N1 vaccine
  - If previous immunity against AH1N1 (Kelly BMC Immunology 2012; 13: 49-58)
  - If second dose (Durier AIDS 2012; 26: [Epub ahead of print])

Pneumococcus vaccine

- The « old » polysaccharidic PPV-23
- « T Cell independant immunity »
- Better response if CD4> 500/mm³ (Dworkin, CID 2001; 32: 794-800)
- Hyporesponsiveness following booster immunization with bacterial polysaccharides is caused by apoptosis of memory B cells (Brynjolfsson J Infect Dis. 2012 ;205:422-30)
- Licensure of the « new » 13-valent pneumococcal conjugate vaccine for adults aged 50 years and older
  - FDA approved PCV13 for prevention of pneumonia and invasive disease among adults aged 50 years and older (MMWR 2012, 61: 394-5)
  - EMEA approved to extend use of Prevenar 13 to adults 50 years and older for the prevention of Invasive Pneumococcal Disease
Pneumococcus vaccine

The effectiveness of pneumococcal polysaccharide vaccination in HIV-infected adults: a systematic review

Rit Pedersen,1 N Libois,2 L Østergaard1 and OS Søgaard1
1Department of Infectious Diseases, Aarhus University Hospital, Skjøby, Denmark and 2UNAIDS, Geneva, Switzerland

Methods
A systematic search of peer-reviewed publications (EMBASE, the Cochrane Library, and PubMed/BioMed Central), the Internet and grey literature was conducted. Three hundred and eighteen documents were reviewed. Studies reporting risk estimates for all-cause pneumococcal pneumonia, all-pneumococcal disease, and/or invasive pneumococcal disease after PCV–23 immunization in HIV-infected adults were included.

Conclusions
The current clinical evidence provides only moderate support for PCV–23 immunization of HIV-infected adults. More data are needed on the efficacy of newer conjugated pneumococcal vaccines, which may be more immunogenic and could potentially replace PPV–23 in the future.

From the ACIP…

- Routine use of PCV7 in infants and young children
  - significant reductions in IPD caused by vaccine serotypes in children, and in adults because of indirect effects
- Rates of IPD caused by vaccine serotypes in non HIV adults aged 18–64 years decreased (6 to 1 case per 100,000 during 2000–2007)
- However the incidence of IPD caused by the serotypes included in PCV7 remained high in HIV-infected persons aged 18–64 years (64 cases per 100,000 persons with AIDS)
- Moreover, 50% of IPD cases among immunocompromised adults in 2010 were caused by serotypes contained in PCV13
- An additional 21% were caused by serotypes only contained in PPV23 (CDC, unpublished data, 2011)
Pneumococcus vaccine

- Studies in HIV adults with PCV7 or 9
  - RCT in Malawi, PCV7 vs placebo: vaccine efficacy for preventing a recurrence of IPD was 74% (French, N Engl J Med 2010; 362: 812-22)
  - PCV7 more immunogenic than PPV23, no benefit of second dose (Feiken, Vaccine 2002; 20: 545-53)
  - On HAART vs HAART naive: more durable antibody response of higher functional activity, independently of baseline CD4 count (Sogaard AIDS 2010; 24: 1313-22)
- Waiting for results of studies on-going with PCV13 …

---

EACS Guidelines
Version 6.1 November 2012

<table>
<thead>
<tr>
<th>Streptococcus pneumoniae</th>
<th>Higher rate and severity of invasive disease</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• In adults use PPV-23 polysaccharide vaccine (22)</td>
</tr>
<tr>
<td></td>
<td>• Consider delaying vaccination until CD4 ≥ 200/µL</td>
</tr>
<tr>
<td></td>
<td>• Consider (single) booster after 5 years (26)</td>
</tr>
</tbody>
</table>

ii 13-valent conjugated vaccine may replace 23-valent polysaccharide vaccine as more immunogenic

iii Repetitive boosting may attenuate immune response
ACIP Guidelines

Pneumococcus vaccination

- **PNEUMO 23®**
  - Vaccination every 5 years
  - Price: 28.40 €

- **PREVENAR 13®**
  - Price: 74.55 €

- Primovaccination by PCV 13 followed by PPV-23 after 8 weeks?
Hepatitis A vaccination

- Very good immunogenicity in general population (98-100% responders after 2 doses) (Cllemens J Infec Dis 1995; 171 (3): S44-9)
- Less better immunogenicity in HIV people (48% responders) (Weissman J Vir Hep 2006; 13: 81-86)
  - Better in female, high CD4, low VL, HAART
- Case of Hepatitis A 2 years after vaccination in MSM (Mor J Infec Dis 2002; 201: 299-303)
  - CD4 551/mm³ while vaccinated
  - No Antibody 2 month prior to the onset
- CD4 551/mm³ while vaccinated

3 doses schedule for CD4 200-500/mm³ (Launay J AIDS 2008; 49: 272-5)

British HIV Association guidelines for immunization of HIV adults 2008
- 3 doses if CD4<300/mm³
  - Based on study in HIV childrens (Weinberg J Infect Dis 2006; 193: 302–11)
- Booster at 5 years for people at risk
- Routine post-vaccination testing is not generally recommended, but may be considered in selected high-risk individuals
Hepatitis A vaccination

- ACIP and EACS: According to risk profile (travel, MSM, IVDU, active hepatitis B or C infection) virtually every HIV patient...
- Vaccine should be provided to all non-immunized HIV-positive individuals (Rosas, AIDS Rev 2007; 9: 173-87)
- Non responders to the HAV vaccine should be revaccinated once their CD4 count has risen, ideally above 500 cells/mm³, in response to HAART (Rosas, AIDS Rev 2007; 9: 173-87)

Hepatitis B vaccination

- 80-90% responders in healthy vaccinated young adults (Francis Ann Int Med 1982; 97:362-6)
- Response rates and HBsAb levels and durability are reduced in HIV-positive people (Biggar N Engl J Med 1987; 316:630-1)
- Response rates range between 7 and 88% and correlate strongly with CD4 count, CD4 count nadir and plasma HIV RNA load (Kung Int J STD AIDS 2006; 17:509-14)
- Rates of achieving HBsAb levels >10 IU/L after standard vaccination are 56–88% at CD4 > 500/mm³, but only 25% or less with CD4 <350–200/mm³
- Although infection can occur in HIV-infected patients who respond to vaccination, it is usually characterized by a mild course and reduced risk of chronicity (also if HbsAb disappears) (Kunzinger Genitourin Med. 1993; 69: 406–7)
Hepatitis B vaccination BHIVA 2008

- The HBsAb level should be measured 6–8 weeks after vaccination. Vaccine recipients with HBsAb <10 IU/L should be offered three further double-doses, given at monthly intervals (B, IIa). Depending on the level of risk, revaccination may be delayed until the CD4 count has risen >500/mm³ on HAART (B, IIa). Retesting for HBsAb is recommended 6–8 weeks after the final vaccine dose (C, IV)
  - Vaccine recipients with an HBsAb response >10 but <100 IU/L should be offered one additional vaccine dose. Responses should be rechecked 6–8 weeks later (C, IV)
  - Following successful immunization, the HBsAb level should be measured yearly. A booster should be offered to persons whose HBsAb levels have declined <10 and ideally <100 IU/L (C, IV)

- B Evidence at level IIa, IIb or III (IIa At least one well-designed controlled study without randomization)
- C Evidence at level IV (IV Expert committee reports or opinions of respected authorities)

Hepatitis B vaccination

- Vaccination with 4 double doses (2 X 20 μg) at 0, 1, 2 and 6 month of 163 patients (Potsch Vaccine 2012; 30: 5973-7)
  - Seroconversion rates similar to those with standard schedule in immunocompetent subjects
  - Higher antibodies titres
  - Better response if VL « undetectable » and if high CD4
  - Randomised trial of recombinant hepatitis B vaccine in 210 HIV-infected adult patients comparing a standard dose to a double dose (2 X 20 μg) 0, 1, 6 month (Fonseca Vaccine 2005; 23: 2902-8)
  - Best current strategy for hepatitis B vaccination in: double doses when the viral load is likely to be low and CD4 ≥ 350/mm³
  - Randomized trial in 437 adults with HIV-1, both the 4 IM double-dose regimen (2 X 20 μg) and the 4 intradermal low-dose regimen improved serological response compared with the standard HBV vaccine regimen (Launay JAMA 2011; 305: 1432-40)
  - 0, 4, 8, 24 weeks
  - As in dialysed patients....
What about Twinrix?

- In 336 HIV-infected youth (12 to 24 years), improved vaccine response with
  (Flynn J Acquir Immune Defic Syndr. 2011; 56:325-32)
  - Engerix B 2 X 20 μg
  - Twinrix
  - Higher baseline CD4

Hepatitis B vaccination

- **EACS 2012**: Consider double dose (40 μg) and intradermal vaccination in non-responders, in particular with low CD4 and high viremia. Repeat doses until HBsAb ≥ 10 IU/L / ≥ 100 IU/L according to national guidelines
- **ACIP 2012**: Adult patients receiving haemodialysis or with other immunocompromising conditions should receive 1 dose of 40 μg/mL (Recombivax HB) administered on a 3-dose schedule or 2 doses of 20 μg/mL (Engerix-B) administered simultaneously on a 4-dose schedule at 0, 1, 2, and 6 months.
- **UptoDate**: double doses at 0, 1, 2 and 6 month if CD4>200/mm³

Fendrix 20μg 54.29€
For doses: 0, 1, 2 and 6 month
New adjuvant MPL (3-o-desacyl-4'-monophosphoryl lipid A) with aluminium phosphate

HBvaxpro 40μg 61.61€
Three doses: 0, 1 and 6 month
Papillomavirus Vaccination

- In non HIV, HPV 16 and HPV18 detected in 71% of ICC (Bruni J Infect Dis 2010; 202: 179-99)
- 2 USA studies of HIV-positive female:
  - In 227 patients, infection occurred more frequently with oncogenic genotypes other than types 16 and 18 (HPV types 58, 53/66, 68/70, and 31/33/35) (Shrestha BMC Infect Dis 2010; 10:295)
- Meta-analysis in 5578 HIV women: proportion of HIV-positive women with HPV16 rose with increasing severity of cervical lesions but HPV16 remained underrepresented in HIV-positive women with HSIL (Clifford AIDS. 2006; 20:2337-44)
- Immunization studied in HIV children or men published, but nothing with HIV women (5 studies on-going http://clinicaltrials.gov)

Papillomavirus Vaccination

**Human Papillomavirus**

<table>
<thead>
<tr>
<th>Shared risk with HIV of contracting infection, higher rate of cervical and anal cancer</th>
<th>Vaccination of women and men according to national guidelines</th>
</tr>
</thead>
</table>
| • ACIP
  - For females, either HPV4 or HPV2 is recommended at 11 or 12 years of age, and for those 13 through 26 years of age, if not previously vaccinated.
  - Recommendations on the Use of Quadrivalent Human Papillomavirus Vaccine in Males (HPV4) (MMWR 2011; 60(50):1705-8)
    - HPV-associated cancers in males include some anal, penile, and oropharyngeal cancers caused primarily by HPV 16
    - Nononcogenic HPV types, primarily 6 and 11, cause >90% of genital warts (condylomata) and most cases of recurrent respiratory papillomatosis
    - Vaccination of 11 or 12 years males (from 9 through 26 years)
    - For immunocompromised males, as for all males through age 26
      - The immune response and vaccine efficacy might be less than that in immunocompetent persons.
    - MSM are at higher risk for infection with HPV types 6, 11, 16, and 18 and associated conditions, including genital warts and anal cancer |
Papillomavirus Vaccination

- Bivalent 16/18 and quadrivalent 6/11/16/18 vaccine
- Synthesis in vitro of L1 proteins

M 0, 2 et 6
112,69€

M 0, 1 et 6
120,54€

Measles, Mumps and Rubella Vaccination

- Live virus!
- 1 case of severe pneumopathy and death in 20 years old HIV patient vaccinated 10 month before, while CD4 count low (CDC, MMWR 1996; 45: 603-§)
- Vaccination is not associated with serious adverse events among HIV without evidence of severe immunodepression (Watson, MMWR Recomm Rep 1998; 47: 1-57)
- No EACS guideline
- Vaccination of « unprotected » if CD4>200/mm³ (BHIVA)
- 2 dosis, one month interval
Varicella Vaccination

- Live attenuated vaccine
- Data mainly extrapolated from pediatric
- 1 case of disseminated disease after vaccination in a child with low CD4
  (Kramer Pediatrics 2001; 108:E39)
- Treatment with acyclovir in case of disease due to vaccine

- Zona vaccine: same live attenuated strain at a 14-fold increased potency. Contraindicated if CD<200/mm³! Not available in Belgium

Varicella Vaccination

- EACS: vaccinate if seronegative and CD4>200/mm³
- ACIP 2012
  - All adults without evidence of immunity to varicella should receive 2 doses of single-antigen varicella vaccine
  - Contraindicated in HIV with CD4<200/mm³
  - Special consideration for vaccination — close contact with persons at high risk for severe disease (e.g., health-care personnel and family contacts of persons with immunocompromising conditions) or — high risk for exposure or transmission (e.g., teachers; child care employees; residents and staff members of institutional settings, including correctional institutions; college students; military personnel; adolescents and adults living in households with children; nonpregnant women of childbearing age; and international travelers).
Typhoid fever Vaccination

- Approximately 50% to 80% efficacy in non HIV
- Impaired antibody response after immunization of HIV-infected individuals with the polysaccharide vaccine against Salmonella typhi (Typhim-Vi) (Kroon Vaccine 1999; 17: 2941-5)
- Typhim-Vi can be considered to be a T-cell-independent type 2 antigen.

Vi Capsular polysaccharide vaccine out of stock!

- Live vaccine seems safe in HIV adults (only 6 of 42 had CD4<200) (Banda Vaccine 2012; 30: 5566-60)
  - But until now contrindicated if CD4 low
Yellow Fever Vaccination

- Live attenuated strain Rockefeller 17D, cultivated on chicken’s embryo
- In HIV negative, 99% of seroconversion rate within 30 days of immunization, and protection may persist for 30 years. *(Poland Bull WHO 1981; 59: 895-900)*
- Immunogenicity lower and shorter in HIV
- Antibody response in 93% of 364 vaccinated HIV after a mean duration of 8.4 years after vaccination. *(Pacanowski J AIDS 2012; 59: 360-7)*
  - Correlated with HIV RNA level and duration of control
  - Useful of Neutralising Antibodies Titer (>= 1/10)
- Vaccination if CD4>200/mm³ *(ACIP MMWR 2002)*

Yellow Fever Vaccination

- HIV negative patient suffering from YF vaccine-associated viscerotropic disease was shown to have polymorphisms in CCR5 and RANTES genes. *(Pulendran J Infect Dis 2008; 198: 500-7)*
- Avoid if maraviroc used. *(Conesa-botella J Infect Dis 2009; 199: 601)*
### 2.3. Adultes et adolescents ≥ 16 ans

<table>
<thead>
<tr>
<th>MALADIES (commentaires)</th>
<th>HIV CD4 &lt; 200/mm³</th>
<th>HIV CD4 200-500/mm³</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaccinations (remarques générales voir 2.4.8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vaccines inactives</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DTpE</td>
<td>S</td>
<td>S</td>
</tr>
<tr>
<td>IPV</td>
<td>R</td>
<td>B</td>
</tr>
<tr>
<td>Haemophilus influenza b</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Hépatite A 2 doses</td>
<td>R</td>
<td>R</td>
</tr>
<tr>
<td>Hépatite B 2 doses</td>
<td>C</td>
<td>C</td>
</tr>
<tr>
<td>Influenza (annuelle)</td>
<td>C</td>
<td>C</td>
</tr>
<tr>
<td>Pneumocoque (23A)</td>
<td>C</td>
<td>C</td>
</tr>
<tr>
<td>Meningo C (conjugué)</td>
<td>5 jusqu'à 18 ans</td>
<td>5 jusqu'à 18 ans</td>
</tr>
<tr>
<td>IPV</td>
<td>R</td>
<td>R</td>
</tr>
<tr>
<td>Vaccines vivants</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BCG (2.4.A)</td>
<td>X</td>
<td>R</td>
</tr>
<tr>
<td>vaccimune (2.4.A)</td>
<td>X</td>
<td>R</td>
</tr>
<tr>
<td>Actiris (2.4.A)</td>
<td>X</td>
<td>R</td>
</tr>
<tr>
<td>Vaccines inactives liés aux voyages</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Encephalite japonaise</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Encephalite européenne par morure de liques</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Filatre typhoïde</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Rage)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Meningite - polioschétique ou conjugué valérien</td>
<td>R</td>
<td>R</td>
</tr>
<tr>
<td>Vaccines vivants liés aux voyages</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- **All patients, 3 doses if CD4<300 ?**
- **3 doses of 40µg or 4 doses of 2X20µg ?**
- **PCV13 & PPV23 after 8 weeks ?**
- **HPV4 for men from 9 through 26 years ?**
- **Vaccination of « unprotected » if CD4>200/mm³ ?**
- **Vaccination of seronegative if CD4>200/mm³ ?**
- **Not available in Belgium**
In conclusion

- Better use inactivated vaccine
- Vaccinate earlier in the evolution of the HIV disease
- CD4 count gives an evaluation of vaccination efficacy; immunization will be less efficient if CD4 below 100-200/mm³
- Undetectable viral load is also a good evaluation of immunity
- Under HAART, 3 to 6 month necessary for immune restoration. Wait if possible
- Possibility for serological monitoring

Thanks' for your attention