Vaccination in asplenic patients

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The spleen

- **Important cleansing and immunological role:**
  - filter small particules out of the blood
    by macrophage of the marginal B zone
    (Ab independent)
  - production of Ab, especially early IgM
    against capsular polysaccharide antigens
The spleen

• Those Ab are necessary to clean the blood from the encapsulated microorganisms outside the spleen (liver, …)

→ *If case of functional or anatomic asplenia:*

  Major risk of severe/rapidly evolving bacterial/parasitic infections
Which pathogens?

- **Encapsulated bacteria:**
  - S.pneumoniae
  - H.influenzae group b
  - N.meningitidis
  - *Capnocytophaga canimorsus*

- **Parasites:**
  - Plasmodium
  - Babesia (USA)

Type of patients

- **Congenital asplenia:** very small group…
- **Surgical removal:**
  
  *severity of consequences linked to:*
  
  - **age** of the patient: less in young adults
  - **reason** for splenectomy: less if trauma
  - **extent** of splenectomy
  - **time after** splenectomy (but…)

- **Functional asplenia:**
Type of patients

- Functional asplenia:
  - underlying condition: sickle cell, cirrhosis, lupus,…
  - specific treatments: irradiation,…

| TABLE 315-2 -- The Risk of Postsplenectomy Sepsis Related to Splenectomy Cause (Cases/100 Patient-Years) |
|---------------------------------------------------------------|-----------------|-----------------|
| **Low Attack Rate**                                           | **Risk** | **N** | **Range** |
| Incidental surgical                                          | 1.17     | 2521  | 1.0-2.4  |
| Idiopathic thrombocytopenic purpura (ITP)                    | 2.03     | 2728  | 1.5-3.3  |
| Trauma                                                       | 2.07     | 6612  | 1.5-2.4  |
| **Intermediate Attack Rate**                                 |          |       |          |
| Spherocytosis                                                | 3.15     | 4836  | 2.4-3.6  |
| Hodgkin's disease                                            | 6.15     | 2507  | 4.1-11.6 |
| Portal hypertension                                          | 6.72     | 610   | 4.1-8.6  |
| **High Attack Rate**                                         |          |       |          |
| Thalassemia                                                 | 11.6     | 852   | 7.0-24.8 |
| Autoimmune lymphoproliferative syndrome                      | 31.310   | 16    |          |
Overwhelming post splenectomy infections (OPSI)

- 500-600x more than in eusplenic patients
  2-5/1000 pat/year
- Majority within the first 2 years...
  but increased risk still there after decades
  (average in a British study: 10 to 20 y) *
- Quickly leading to MOF/death in few hours
  \( \rightarrow \) Mortality \( \geq 50\% \) \( \rightarrow 80\%.. \)

...with 90\% of all due to pneumococcal infection

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Figure 315-3 The interval from splenectomy to postsplenectomy sepsis. Of the total \( N = 288 \), 3.1\% occurred more than 20 years after splenectomy.
**Overwhelming post splenectomy infections (OPSI)**

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  but increased risk still there after decades
  
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- Quickly leading to MOF/death in few hours
  
  → Mortality ≥ 50% (→ 80%..)

...with 90% of all due to pneumococcal infection

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*Figure 315-4 A,* The Gram stain of a buffy coat smear from a patient with rapidly fatal pneumococcal postsplenectomy sepsis, 7 years after a staging laparotomy for Hodgkin’s disease, showing many gram-positive diplococci. *B,* A more magnified Wright stain of a peripheral blood smear from the same patient, showing extracellular diplococci. *(From Lynch AM, Kapila R. Overwhelming postsplenectomy infection. Infect Dis Clin North Am. 1996;10:693-707. Used with permission of the publisher.)*
Microbiology of OPSI

- **S.pneumoniae** in (80) to >> 90% of cases
  - Increase with increasing age
  - Same distribution of serotypes than in other IPD
- **H.influenzae type b:** < 10%
  - Mostly (90%) in < than 15 y old
  - ↓↓↓ with generalized vaccination
- **N.meningitidis:** occurs, but same v/severity than in eusplenic patients (same in mice model)

Figure 315-5 The microbiology of postsplenectomy sepsis based on 298 culture-positive episodes including those due to the meningococcus. Of the total, 51 (14.6%) additional episodes did not have a reported organism. Data are not stratified by age or cause of splenectomy.

Is an infection protecting from others?

- No!
- When a repeat infection:
  - 61% of second
  - 84% of third
  Occur within 6 months after the first episod

Are there recent studies of pneumo vaccination in asplenic patients?

- Yes
  - Comparison of PCV7 (x2) +PSPV23 (x1)
    and PSPV23 alone
    Same level of IgG (Elisa) BUT
    significant improvement in OPA
    with the combined schedule
    Vernacchio et al JID 2000
Are there recent studies of pneumo vaccination in asplenic patients?

• Immunogenicity of PCV7 (x3) +booster PSPV23 at 15/18 months in **infants** with SCDisease
  ≥ 95% of high Ab titers for the 7 serotypes
  +good booster activity
  Reinert et al Ped Inf Dis J 2007

• Revaccination of children with asplenia, previously vaccinated with PSPV23 ≥3y before
  →PCV7 leading to better immunological response than PSPV23
  Smets et al Vaccine 2007

Clinical proof of pneumo vaccination efficacy?

• No
  -Comparing ‘58-’70 and ‘77-’95 in asplenic children of Toronto: ↓ 48% in OPSI
    !mixed of AB prophylaxis and vaccination…

  -Hospitalization for IPD in a national sample of children with SCD before/after PCV7 licensure
    →threefold reduction
  Mc Cavit et al Ped Blood Cancer 2012
Hib vaccine in adults with asplenia

- Vaccine is immunogenic
- Lower level of Ab (Cimaz JID 2001)
- No recommendations for booster

Guidelines for infection prevention in individuals with (functional) hyposplenia and asplenia

February 2012
Guidelines in Holland

- **Pneumo**: Conjugate vaccines are preferred
  If both advised, start with the conjugate
  - Children: 6-16: 2 doses PCV with 1 month interval and PSPV23 ≥ 8 weeks later
  - Adults: PCV once, and PSPV23 once (to repeat once after 5 years)
- **Hemophilus**: adults: once
- **Meningococci**: once
- **Influenza**: every year

Haut Conseil de la santé publique

AVIS

Relatif aux recommandations vaccinales spécifiques des personnes immunodéprimées ou aspléniques

16 février 2012
Guidelines in France

• « …les vaccins non conjugués…sont peu immunogènes et leur efficacité diminuée chez ces patients devrait faire préférer l’utilisation de vaccins conjugués »

• Recommend:
  - PCV
  - Meningo C or 4V (once in adults)
  - H.influenzae (once in adults)
  - Influenza (every year)

Guidelines in the USA

• October 2012; MMWR (based on ACIP 6/2012)
  PCV13 recommended in immunocompromised adults (GRADE A)
    including functional or anatomic asplenia
    + one dose of PSPV23 ≥ 8 weeks later
      (to repeat once after 5 years)
  NB: if PSPV23 already received, PCV13 ≥ 1 y later
Recommendations US: ACIP

Use of 13-Valent Pneumococcal Conjugate Vaccine and 23-Valent Pneumococcal Polysaccharide Vaccine for Adults with Immunocompromising Conditions: Recommendations of the Advisory Committee on Immunization Practices (ACIP)

<table>
<thead>
<tr>
<th>Risk group</th>
<th>Underlying medical condition</th>
<th>PCV13 Recommended</th>
<th>PPSV23 Recommended</th>
<th>Revacination 5yrs after first dose</th>
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<td>ImmunoCOMPETENT PERSONS</td>
<td>Chronic heart disease†</td>
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<td>Solid organ transplant</td>
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Guidelines in the USA

- In addition to:
  - Hemophilus: once in adults
  - Meningo: once (4V) in adults
  - Influenza: every year
Other countries

- Similar guidelines in:
  - Germany (last in July 2012)
  - UK
  - Australia and New Zealand
      …..

Proposed Belgian Guidelines

- Recommended vaccines are:
  - **Pneumo**: *
  - Meningo: C in children (as usual),
    4V in adults (and in children?)
  - Hemophilus: as usual in children
    once for adults
  - **Influenza**: annually
Proposed Belgian Guidelines

• *Pneumococcal vaccination:*

  - *Children:*
    - 2-12 months: PCV13 (x3, with 8w interval)
      + PCV13 at 12 months
      + PSPV23 at 24 months
    - 12-5 y: PCV13 (x2, with 8 w interval)
      + PSPV23 at/after 24 months
    - > 5 y: PCV13 once + PSPV23

  NB: PSPV23 to repeat every 5 years

• *Pneumococcal vaccination:*

  - *Adults:*
    - PCV13 once
      + PSPV23 ≥ 8 w after

  NB: PSPV23 to repeat every (3)-5 years
Serotype coverage of PCV 13 and PSPV23 in Belgium

- From surveillance data obtained in IPD from 2009 to 2011 in 44% of all acute hospitals
- PCV13: 60-65%
- PSPV23: 85-90 %
  for patients < 75 y

Coverage by age
17

Proposed Belgian Guidelines

- Recommended vaccines are:
  - Pneumo:
  - Meningo: C in children (as usual), 4V in adults (and in children?)
  - Hemophilus: as usual in children once for adults
  - Influenza: annually
Influenza vaccination

• Influenza is not more severe in asplenia
  BUT
  Influenza facilitates bacterial infections
  (especially pneumococcal infections)
  that could be more severe

→ Therefore, asplenic patients should be vaccinated annually

When should we vaccine?

• Whenever possible, to be completed
  at least 2 weeks before the procedure
  OR ≥ 2 weeks after
Based on data from Shatz et al with PSPV23:
  - similar Ab levels (Elisa) to control patients
  - lower functional Ab activity
    if vaccination D 1 or 7 postop
  BUT similar to control if D 14 or D 28
  J Trauma 1998 and 2002
Thank you for your attention!